General practitioner on an island

Jacobs, Jacobus Johannes Wilhelmus Maria

General practitioner on an island

How research and innovation help to improve primary care

Jac. Jacobs

Photography: **Sybren Sikma**

Printed by: **Chris Russell, Groningen**

ISBN: 978-90-367-8816-8

rijksuniversiteit groningen

General practitioner on an island

How research and innovation help to improve primary care

Proefschrift

ter verkrijging van de graad van doctor aan de
Rijksuniversiteit Groningen
op gezag van de
rector magnificus prof. dr. E. Sterken
en volgens besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op

woensdag 1 juni 2016 om 16.15 uur

door

Jacobus Johannes Wilhelmus Maria Jacobs

geboren op 8 mei 1956
te Beers

Promotores

Prof. dr. R. Sanderman
Prof. dr. T. van der Molen

Beoordelingscommissie

Prof. dr. N.H. Chavannes
Prof. dr. J.C. Coyne
Prof. dr. C. Lionis

Contents

Chapter 1

General introduction

Background

Family medicine in the Netherlands (see Box 1) is acknowledged worldwide for its high quality [3,4,5]. This is due, in part, to the uniform care provided by general practitioners (GPs). Arguably, treatment guidelines are very advanced in the Netherlands. The introduction of comprehensive guidelines in 1986 was intended to support the daily practice of GPs. They have been specifically developed by GPs to cover the most common presentations to primary care, and are based on consensus opinions by general practitioners and clinical specialists [6]. Today, some 100 guidelines exist that are updated on four- or five-yearly cycles. In 2000, the Dutch College of General Practitioners received the Carl Bertelsmann prize [7] for this approach to care standardization.

Box 1

The Dutch healthcare system is divided into primary, secondary, and tertiary care. These three tiers correspond to general practice, hospital care, and specialized laboratories or university medical centers, respectively.

General practitioners (GPs) form the bulk of primary care. Moreover, GPs are gatekeepers to the other levels of care, with referral only usually possible via a referral from a GP or another member of primary care.

Primary care, including general medical care by GPs, is accessible and is offered close to home for the majority of patients in the Netherlands [1].

Primary care in the Netherlands is the key to efficient care. In 2011, primary care cost 3 % of total health care spending, with GPs managing 90% of all health care needs [2]. The corresponding figures were 3.5% and 95% in 2012.

Although the aim of the professional (LHV: *Landelijke Huisartsen Vereniging* or National GP association) and scientific (NHG: *Nederlandse Huisartsen Genootschap* or Dutch college of general Practitioners) association is for GPs to cooperate in research by 2022 [3], such practice is rare at present [13]. At this time, only 5% of Dutch GPs in training are working on a PhD program [3]. These PhD programs are often part

of large-scale major research projects that are undertaken in the setting of academic GP university departments with specialist interests. The Dutch College of General Practitioners recently indicated that the scientific basis for the general practice guidelines has gaps and redundancies because of this specialized secondary-care focus of research, with insufficient evidence from primary care itself [14]. Mackenzie [15] came to the same conclusion in 1908, seeing an important role for research by GPs in their own to supplement large-scale specialist research, and arguing that the "progress of medicine will be hampered and delayed till the GP becomes an investigator." He therefore expected significant progress to occur in the development of family medicine through practice-based research [15, 16]. Green and Hickner (2006) have also mentioned research pioneers like Pickles, Fry, Huygen, and Hames "who demonstrated that important new knowledge, not otherwise accessible, could be discovered by the practicing family physician." Furthermore, such research has been a good basis for further large-scale studies in primary care research networks [5]. When gaps exist in the available evidence base, the comments offered by Mackenzie remain as applicable today as they did when he first made them, and GPs must aim to find answers themselves to the questions they face in daily practice [16].

In this way, GPs can contribute to medical practice in primary care, improve the development of the profession, and increase our knowledge of disease processes. Indeed, research contributions need not be limited to clinically oriented problems. GPs have important roles in public health and have a social responsibility to implement new developments in health care that are both adequate and cost-effective [3]. These require epidemiological and cost-benefit approaches, respectively.

In this thesis, a number of cases are followed that show how research questions can be explored and answered in the primary care setting. Specifically, there is a description of the aspects of family medicine in Ameland, a remote area (see Box 2) with different disease characteristics where the large distances from hospital have required innovative care solutions.

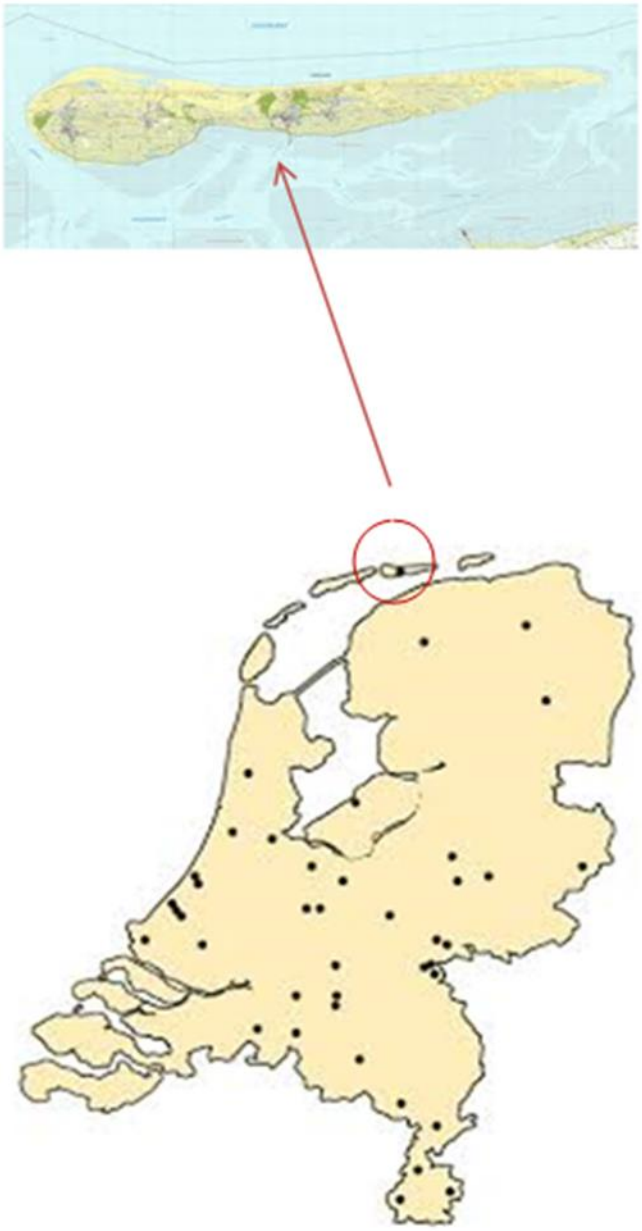
Box 2

Ameland

Ameland is one of the five Frisian Islands to the north of the Netherlands. It comprises 58 square kilometers (56% open natural terrain) with 3500 inhabitants, 30,000 beds for tourists, 4000 seasonal workers, and a significant amount of daytourism (approximately 65,000 persons on the island at peak days) [(17)].

Six times per day, a ferry sails from Ameland to Holwerd (main land) and vice versa. The ferry trip takes about one hour.

Health care is provided by two family practices with four GPs. In emergencies, two ambulances are available with trained nurses. The island has no hospital, with the nearest being on the main land. When a patient has to go to the hospital for further diagnosis or therapy, they must travel via the normal ferry. Visiting a hospital can therefore take an entire day. In case of an emergency, he or she are transported via the Safe And Rescue (SAR) Helicopter (based at Leeuwarden), the trauma helicopter (based at UMCG Groningen), or a fast boat (available on Ameland). A patient can be in the hospital within 40 minutes (fast boat plus ambulance) or in one hour and 15 minutes (SAR or trauma helicopter).



Peculiarities of island-based care

A particular issue is that the physical distance to the hospital renders the `golden hour' after an emergency even more critical, particularly when emergency treatment is not feasible at the hospital within that time. Thus, GPs may prefer to start treatment early to prevent delays and complications, and to avoid unnecessary referrals and traveling time to the hospital.

An urban–rural health disparity exists due to the location of Ameland. Its open natural terrain makes ticks more prevalent, specific guest accommodation (such as recreational farms) make gastro enteritis and respiratory infections more prevalent, and the distance to a hospital and absence of additional diagnostic facilities make the management of emergency situations difficult. Therefore, a GP on an island like Ameland is sometimes forced to improvise, to initiate additional epidemiological research, to deviate from the guidelines of the profession, and to make novel provisions. Implemented efficiently, they can enable earlier diagnosis and treatment, in some cases leading to the provision of secondary-care services in primary care.

In this thesis, three case studies are presented to illustrate specific problems confronted by GPs on Ameland, and how they were resolved. The first two, ticks and "the Amelander Krankheit," were specific to the island. The third issue was related to patient management when located at a considerable distance from hospital, where teleradiology was found to be suitable for the management of fractures in general practice.

Research questions

Amelander Krankheit

Because of the island location and variable tourist population, some diseases have occurred with regularity that rarely present on the mainland [18]. In the summer season, recreational farms are used as a residence for between 20 and 120 German children (aged 12–18 years) per farm with 10 to 15 adult supervisors. The children sleep in a single room in the stables, and due to the large number of children in a relatively confined space, diseases such as impetigo, respiratory infections, gastroenteritis (e.g., noroviruses) and childhood diseases regularly occur. Indeed, there have been frequent epidemics of measles, chicken pox, scarlet fever, mumps, and whooping cough. On one occasion, there was a meningitis outbreak.

Dealing with epidemics is generally simple. In most cases, public health services or a health inspector is called, and these consult their records and provide recommendations that aim to prevent major complications and spread. However,

problems arise when there is a public health threat for which authorities cannot provide informed advice. This happened with a gastroenteritis outbreak in German children that could not be explained initially. In the German region of Cologne, many children were reported to suffer from gastroenteritis following trips to Ameland, which became known as the "Amelander Krankheit." It appeared that children were infected with campylobacter at some farms, for which there was no good explanation. In Chapter 2, the investigation into the so-called Amelander Krankheit is described.

Research question: What caused this "Amelander Krankheit"?

Ticks

Long before Lyme disease was described in the medical literature [19], it was known that diseases in the dunes of Ameland existed that might be associated with ticks.

Box 3

My personal experience

My neighbor (born in 1925) told me that as a child he was never allowed to play in the dunes. The dunes were dangerous because there were diseases. A tourist (born in 1918) who visited the island annually from childhood until today, told me that in the past his father always had a hipflask of gin with him. If they had played in the dunes in the day, a body check was carried out later; and if a tick was found, the father poured gin in the bottle cap and put this cap overhead the tick. The gin released the tick from the body and the skin was freed from the tick without touching or compressing it.

In the Second World War, rehabilitation homes for Germans soldiers injured on the eastern-front were situated in the dunes. Both then, and in the immediate post-war period when mass tourism started, the risks associated with the dunes were denied by most of the islanders and guests. Indeed, tourists and islanders alike were given little information about the risk associated with the ticks in the dunes, especially those who worked in the dunes [20]. In 1972, a veterinarian detected a spirochete (Borrelia) in a tick taken from a diseased sheep, and he suspected that there was a relationship between this Borrelia species and the sick sheep [21, 22].

In contrast, by the 1990s, after the discovery of the mysterious Lyme disease, there was a strong belief that there was a very high risk of Borrelia Burgdorferi transmission and the development of Lyme disease after a tick bite, and that this was especially the case for ticks bites incurred in the dunes [23, 10]. Even the popular press highlighted the high risk of Lyme disease after a tick bite, without mentioning the precise risk. The turmoil worsened after the discovery of other tick-borne diseases (TBD), such as Rickettsiosis, Babesiosis, and Ehrlichiosis [24]. Such was the magnitude of the problem that it formed a threat to public health. Two solutions were therefore proposed: either to avoid the dunes altogether or to remove the ticks in the correct manner. The last option forms part of the guidelines published by the National Institute for Public Health and the Environment (RIVM). In Chapters 2 and 3 efforts to manage this risk are discussed together with the details of an investigation to determine whether ticks responsible for bites were infected.

Research question: Are ticks in the island infected by Borrelia and other microorganisms? What is the transmission risk?

Teleradiology

The distance to hospital and the desire, among GPs and patients alike, to avoid unnecessary travel through inappropriate referrals, has meant that the threshold for referral and probability of a missed diagnosis is increased. Both inappropriate referrals and missed diagnoses can be fatal for the patient, for example a missed breech presentation, placenta praevia, or twins in obstetrics, or myocardial infarction and arrhythmia in cardiology. However, an incorrect referral has significant direct and indirect costs for both the patient and the healthcare service. Moreover, without additional diagnostic facilities, GPs are infrequently unable to act adequately in the so-called golden hour.

Since July 2007, GPs on Ameland have had access to a teleradiology service. In the Netherlands, like in most advanced countries, all patient x-rays are examined by radiologists. Therefore, it is standard practice that patients requiring x-rays either go to a hospital or to a diagnostic center for imaging. The x-ray facility on Ameland is located in one of the general practices and is available to all patients, including tourists and those from other practices. X-rays are indicated for trauma (e.g., fractures) and non-trauma (e.g., hip, knee, or lung) in preparation for surgery (e.g., cox arthrosis) or for control by a pulmonologist (e.g., lung carcinoma). X-rays are obtained by a radiographer and are digitally transmitted to the hospital on the mainland. Evaluation and interpretation of x-rays are the responsibility of a radiologist or a surgeon; they are available 24 hours a day, 7 days a week, in emergencies and during the daytime for non-emergencies. The radiologist responds

digitally on the same day and, if necessary, directly by phone. Then, in consultation with the surgeon, it is decided whether the patient needs to be treated at hospital or whether they can be treated by the GP on the island under specialist supervision.

Quality control and safety are important consideration. Therefore, radiologists often give instructions to the radiographer by phone, and regularly provide feedback regarding the quality of the x-rays. Additionally, the radiographer receives annual training at the hospital to remain familiar with the hospital's protocols. Concerning safety, the GP is trained as a radiation expert and, together with the Institute of Nuclear Services for Energy, Environment, and Health, is responsible for radiation hygiene and safety. The costs of the X-rays and the honorarium of the radiologist are covered by the patients' insurance companies.

In Chapters 5, 6 and 7, we discuss the introduction of teleradiology on Ameland in more detail.

Research question: What are the consequences of introducing teleradiology in terms of fracture diagnostics and treatment, patients' opinions and cost and benefits?

Outline

The thesis consists of two parts. Part 1 deals with key epidemiological considerations, responding to the following specific questions: Are ticks on Ameland infected by Borrelia and other microorganisms? What is the transmission risk? What caused the Amelander Krankheit? Conversely, Part 2 discusses the role and consequences of the introduction of teleradiology on the diagnosis and treatment of fractures, with specific regard to patients' opinions and the costs and benefits.

Part 1 consists of three chapters. Chapter 2, the results of a study conducted with the GGD (*Gemeentelijke GezondheidsDienst* or Municipal Health Services) Solingen are presented, in which we identified a possible explanation for the so-called Amelander Krankheit'. In Chapter 3, the investigation into the risk of Lyme disease following a tick bite is outlined, providing evidence that Dutch ticks have shown a high prevalence of *Borrelia Burgdorferi* and *Rickettsia Helvetica* carriage, and that they can contain Babesia, Anaplasma, and Ehrlichia species. In Chapter 4, the risk of these TBDs following a tick bite is also discussed. In Part 2 consists of three chapters. Chapter 5 presents the outcomes of a retrospective, observational study on the impact of the introduction of teleradiology on diagnosis and therapy. Specifically, all traumas in 2006 (without teleradiology) are compared with those in 2009 (with teleradiology). In Chapter 6, a cost-benefit analysis of teleradiology is provided to

compare the costs with and without teleradiology. Chapter 7 summarizes the results of a patient satisfaction inquiry into the use of teleradiology.

Finally, Chapter 8 summarizes the main findings of the thesis, and discusses future research.

References

1. Boot, JMD, **Organisatie van de gezondheidszorg**, Uitgeverij van Gorkum tweede herziene druk, 2010. (Dutch).
2. Statistics Netherlands (CBS) 2011. (Dutch)
3. NHG-LHV **Toekomstvisie huisartsenzorg; modernisering naar menselijke maat**. Huisartsenzorg in 2022. Utrecht 2012. (Dutch)
4. Giesen P, Smits M, Huibers L, Grol R, Wensing M. **Quality of After-Hours Primary Care in the Netherlands: A Narrative Review.** *Ann Intern Med* 2011 Jul 19; **155**(2): 108–13.
5. Green LA, Hickner J**. A Short History of Primary Care Practice-based Research Networks: From Concept to Essential Resarch Laboratories.** *JABFM* January-February 2006; **19**: 1.
6. NHG-standaarden (These guidelines are intended to support the medical policy in the daily practice of the GP).
7. Carl Bertelsmann Preis:Mit dem Carl Bertelsmann Preis zeichnet die Bertelsmann Stiftung innovative Konzepte und exemplarische Lösungsansätze in gesellschaftlichen und politischen Problemfeldern aus und sucht dafür weltweit nach interessanten Vorbildern. (With the Reinhard Mohn Prize the Bertelsmann Stiftung honors innovative concepts and exemplary approaches in social and political problem areas and searches worldwide for interesting examples).
8. Pijnenburg AC, Glas AS, De Roos MA, Bogaard K, Lijmer JG, Bossuyt PM, Butzelaar RM, Keeman JN. **Radiography in acute ankle injuries: the Ottawa Ankle Rules versus local diagnostic decision rules.** *Ann Emerg Med* 2002 Jun; **39**(6): 599–604.
9. Landelijk Protocol Ambulance 8. (Dutch)
10. Wielinga PR, Gaasenbeek C, Fonville M, Boer de A, Vries de A, Dimmers W, Akkerhuis Op Jagers G, Borgsteede F, Giessen van der J. **Longitudinal Analysis of Tick Densities and Borrelia, Anaplasma and Ehrlichia Infections of Ixodes ricinus Ticks in Different Habitat Areas in the Netherlands.** *Appl Environ Microbiol* 2006; **72**: (120: 7594).
11. Dijkstra F, Hoek W vd, Wijers N, Schimmer B, Rietveld A, Wijkmans CJ, Vllema P, Schneeberger PM, **The 2007–2010 Q fever epidemic in the Netherlands: characteristics of notified acute Q fever patients and the association with dairy goat farming.** *FEMS Immunol Med Microbiol* 2012; **64**: 3–12.
12. De Friesland zorgverzekeraar. **Spiegelinformatie 1992 t/m 2010.** (Dutch)
13. Houwelingen A v, Scherptong-Engbers M, Ruijter W de. **Huisarts-onderzoeker wordt node gemist.** *Med Cont* 2013; **5** 1134–1135. (Dutch)

14. Maassen H, **Kennislacunes huisartsgeneeskunde geïnventariseerd**. *Med Cont* 2014; 41: 7, Oktober 2014. (Dutch)
15. Moorhead R. **Sir James Mackenzie (1853–1952): Views on general practice education and research.** *J R Soc Med* 1999; **92**: 38–43.
16. Bremer GJ. **Hora Est. Proefschriften van Huisartsen 1900–1995**. Erasmus publishing.(Dutch)
17. CBS, Gemeente op maat Ameland. (Dutch).
18. Lisdonk vd EH, Bosch vd WJHM, Lagro-Janssen ALM, Schers HJ. **Ziekten in de Huisartsenpraktijk [Illnesses in General Practice]**. Reed Business, fifth revised version 2008. (Dutch)
19. Steere AC, Malawista SE, Snydman DR, et al. **Lyme arthritis: an epidemic of oligoarticular arthritis in children and adults in three Connecticut communities.** *Arthritis Rheum* 1977; **20**: 7–17.
20. Houwerzyl J, Root JJ, Hoogkamp-Kostanje JAA. **A Case of Lyme disease with cardiac involvement in the Netherlands.** *Infection* 1984; **12**: 358.
21. Schildhorn van Veen T. Leyendekker G. **Borrelia theileri (Laveran 1903) in cattle in the Netherlands.** *Tijdschr Diergeneeskd* 1971; **96**: 1028–1031. (Dutch)
22. Kommerij R, Schildhorn van Veen T, Vernooij J. **Koppeldiagnose en behandeling van door teken overgebrachte ziekten op Ameland.** *Tijdschr Diergeneeskd* 1971; **96**: 1326–1329. (Dutch)
23. Uilenberg G, Hinaidy HK, Perie NM, Feenstra T. **Borrelia infecions of ruminants in Europe**. *V Quart* 1988; **10**: 1, 63–67.
24. Sprong H, Wielinga PR, Fonville M, Reusken C, Brandenburg AH, Borgsteede F, Gaasenbeek C, van der Giessen JW: **Ixodes ricinus ticks are reservoir hosts for Rickettsia helvetica and potentially carry flea-borne Rickettsia species**. *Parasit Vectors* 2009; **2**: 41.

PART I

Epidemiology

Chapter 2

Ill after drinking untreated milk – the Ameland disease

Published in Dutch with original title:

Ziek na het drinken van rauwe melk *'Die Amelander Krankheit'*

Jac. J.W.M. Jacobs , Robbert Sanderman

Ned Tijdschr Geneeskd 2013;157 (51): A7078

Introduction

For centuries now, practically everyone has been convinced that milk consumption is good for you. In the western world, milk consumption rarely leads to illness except, for instance, in cases of cow milk allergy. However, the consumption of raw milk can still lead to illness. In the following, we describe four recent cases of illnesses caused by consumption of raw milk. Three with the so-called Ameland disease (in German: *die Amelander Krankheit),* we show how the illness earned its name and one patient with rheumatic complaints.

Patients A, B and C are 3 adolescents 15, 16 and 16 years of age, respectively. They presented at a general practice in the village of Ballum with complaints of stomach ache, cramping and diarrhea with blood. Ballum is located on Ameland, a Frisian island in the north of the Netherlands. The children were vacationing on a recreational farm (i.e., a farm which is in the past a cattle farm in wintertime and is tourist farm in summertime. Today it is tourist farm during the whole year).

The patients reported having drunk raw milk from a cooling tank located on the farm a few days prior to the onset of symptoms. This was done with the permission of the farm owners.

Physical examination showed a slightly elevated temperature of 38.4°C (on average) a swollen abdomen and very active peristalsis. The three patients had no history of illness. We collected a feces culture, and the patients were put on a diet of oral rehydration before slowly introducing solid food. The camp counsellors were given strict instructions to watch over the kids, also at night, to ensure the prevention of life-threatening dehydration. A few days later, the patients were free of complaints. The feces cultures were positive for *Campylobacter jejuni*.

Patient D, a 45-year-old dairy farmer also on the island of Ameland, consulted for inflammation of the knee, elbow and hand joints. The inflammation was accompanied by stiffness of the limbs lasting over an hour in the morning. The complaints of patient D were not preceded by any flu symptoms or other anamnestic signs, such as a tick bite or psoriasis. The patient had no history of illness although hemochromatosis was known to occur in the family.

Upon presentation, we saw a man who was not sick but had a red, swollen, warm right knee which was painful when pressed. The results of blood testing showed no deviations. When referring the patient to a rheumatologist, he mentioned occasionally drinking raw milk. He reported taking a mug of milk from the milk tank on his farm every now and then when the weather was extremely warm. He knew that

he was supposed to boil the milk before drinking it but reported not doing this because his father drank the same raw milk every day and never had complaints.

The feces culture turned out to be positive for *Yersinia enterocolitica,* sensitive to the antibiotics ciprofloxacin and co-trimoxazole.

The dairy farmer was treated with co-trimoxazole, and the complaints disappeared.

History

The 4 cases with different symptoms described in the preceding all involved the same culprit: the consumption of raw milk. For most doctors, the consumption of raw milk is not an obvious cause to consider for an illness. Just how we came to consider the consumption of raw milk in connection with the aforementioned four cases is described in the following.

Germany 1958-1995

Between the years of 1958 and 1995 in the area around Cologne (Germany), there was always a group of children who suffered the following symptoms during summer: malaise, nausea, fever and diarrhoea with sometimes blood in it. The symptoms would generally disappear on their own. In most cases, oral rehydration was prescribed to prevent dehydration. The children who were severely sick were admitted to hospital for observation. And the feces cultures revealed the presence of the *Campylobacter jejuni* bacteria.

It was striking that this illness only affected children. Even more striking was that all of the children had been vacationing on the Dutch island of Ameland in the weeks prior to the occurrence of the symptoms. Hence the name *die Amelander Krankheit* in Germany.

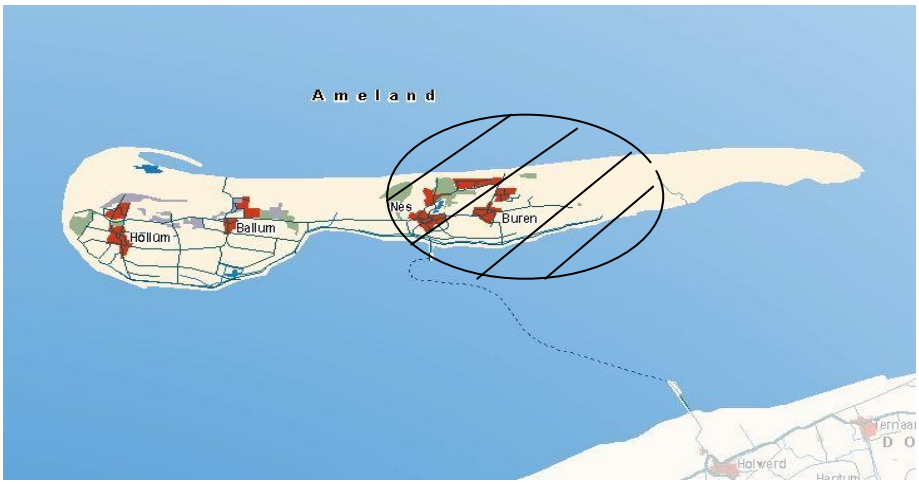
When an increase of hospitalizations occurred in 1993, a public health threat was declared and the German Primary Health Care Service in the city of Solingen initiated an investigation into possible causes. In the fall of 1994, the German Primary Health Care Service contacted the general practitioners on the island of Ameland with some results which they could not explain. What they had found was that that *die Amelander Krankheit* public health threat only occurred in Catholic children who had stayed at recreational farms on Ameland. No adults, counsellors or children who had camped with their parents at a different location within the same region or

Reformed Protestant children who had stayed at recreational farms on Ameland were amongst the patients.

Ameland 1990s

In the 1990s, some 30,000 German children between the ages of 8-18 travelled to Ameland to stay on a total of 60 recreational farms during the summer. Every 3 weeks, 100-120 new children and counsellors would arrive per farm. The children came from underprivileged sections of the Ruhr area of Germany. Their vacations were sponsored by churches, charities and the national health insurance system. Expenses had to be kept to a minimum, and all groceries were brought by truck from Germany to Ameland — with the exceptions of milk and potatoes. The vacation meals were prepared by the German personnel. The Catholic vacation camps were located on the eastern part of the island; the Reformed Protestant vacation camps were located on the western part of the island.

Figure 1: Localisation gastro-enteritis



Many German children stayed on Ameland during their summer vacations in the 1990s. Only the children who stayed on the recreational farms in the east (as indicated in Figure 1) became sick as a result of drinking raw milk.

At the time, Ameland had two general practices serving all islanders and tourists. The doctors from these practices were thus responsible for the care of all patients on the island. In the summer, they regularly saw patients suffering from gastroenteritis, indicating a summer flu which generally responded well to oral rehydration. Sometimes the flu was accompanied by diarrhoea with blood in it. And in the cultures

taken for such cases in the 1990s , the results always revealed infection with *Campylobacter jejuni*. Most remarkable, however, only German patients were infected with the bacteria.

The German counsellors staying on Ameland believed that raw milk consumption had preventive health effects. They therefore required the children on the recreational farms to consume a glass of raw milk each day before eating breakfast. Children with lactose intolerance and a written doctor's statement attesting to this were exempt. For the children staying on the Reformed Protestant farms, the personnel retrieved raw milk from the west side of the island (i.e., from where the farms were located). For the children staying on the Catholic farms, this was done from the east side of the island. The children on both sets of farms consumed raw milk. But only the children staying on the Catholic camps were afflicted with the disease in the end.

Analysis of the milk and feces of the cows supplying the raw milk showed only the cows from the eastern part of the island to be infected with *Campylobacter jejuni*. One can speculate as to how the cows in this area got infected: contamination of the drinking water, bird contamination of their feed or spread of the bacteria from other life stock are among the possibilities [(1)].

Discussion

As described above, raw milk can be contaminated with *Campylobacter jejuni*[(1-2,)] the originator of — amongst other illnesses — gastroenteritis. Raw milk can also be contaminated with *Yersinia enterocolitica*[(3),] which caused the reactive arthritis in patient D (i.e., a familiar post-infection complication, particularly in adults). Raw milk can also contain the following pathogens: *Escherichia Coli O157:H7, Coxiella burnetii*[(4)], *Brucella, Bacillus cereus, Listeria monocytogenes, Mycobacterium aviam* subsp. *paratuberculosis, Mycobacterium bovis, Salmonella* spp. or *Staphylococcus aureus*. These pathogens are usually eliminated by pasteurization or sterilization of the milk. However, consumption of insufficiently cooled milk or milk which exceeds the expiration date can still cause contamination [(5)].

In the Netherlands, pasteurized or sterilized milk is available for human consumption either from a bottle or a carton. If someone wants to drink raw milk, this must first be boiled as laid down in article 8 of the 1994 Commodities Act – Hygiene of Food (section 5: Raw Milk). Since the passage of this act, the area around Cologne has been free of *die Amelander Krankheit*, moreover.

We have not been able to determine how many people actually get sick from the drinking of raw milk in the Netherlands. There are, however, numbers available from the United States (US) where the sale of raw milk is legal in some states but quality control is very strict there. The sale of raw milk is prohibited in other states where producers are required by law to pasteurize the product prior to sale. Between 1993 and 2006, a total of 121 disease outbreaks related to dairy products in 30 states across the US. Out of the more than 4400 patients involved, 236 (5%) had to be hospitalized and 3 of these died. There were twice as many outbreaks in states where raw milk was sold legally (and there were strict quality control checks) with similarly more hospitalizations in these states than in states where the sale of raw milk was prohibited and the milk thus pasteurized. The greater number of hospitalizations in precisely the states allowing the sale of raw milk can be explained in terms of the diseases caused by the pathogens in pasteurized but otherwise contaminated milk (norovirus, *Staphylococcus aureus*), which tend to have a less violent course than the diseases caused by the pathogens found in raw milk (*Campylobacter jejuni, Escherichia Coli O157:H7*)[5]. Even the strict screening of raw milk for the presence of pathogens in the US has not thus led to a decrease in dairy-related disease outbreaks. The inspection of raw cow milk apparently cannot replace the pasteurization or boiling of it prior to consumption. This is a strong argument against the consumption of raw milk — particularly by those who are already at a higher risk of health complications arising from the pathogens sometimes found in raw milk and thus pregnant women, immunocompromised patients and small children [6].

Conclusion

We have all grown up with the idea drinking milk is healthy. The incidences of illness described here show that this is not always the case. Given that milk today is generally pasteurized or sterilized prior to consumption, the drinking of raw milk is not frequently thought of as a possible cause of disease. For patient D, the consumption of raw milk appears to be the family norm, which suggests that the parents of the patient have most likely developed some form of immunity. For the German children, it was difficult to identify milk as the culprit because the disease broke out elsewhere (in Germany) and because the spread of the disease source on the island was abnormal. The spread of the disease source was confined to only the east side of the island.

The consumption of raw milk will continue to occur in the Netherlands. Patients A through D are proof of this. Visitors to the increasing number of cheese-making farms

with an educational character (i.e., for school excursions) may also possibly drink raw milk. Our advice is therefore for patients presenting with gastroenteritis or rheumatic complaints to consider the drinking of raw milk as a possible cause of the complaints.

References

1. Hopkins RS, Olmsted R, Istre GR. **Endemic Campylobacter jejuni Infection in Colorado. Identified Risk Factors.** *American Journal of Public Health* March 1984, **74**, No.3.
2. Evans MR, Roberts RJ, Ribeiro CD, Gardner D, Kembrey D. **A milk-borne campylobacter outbreak following an educational farm visit.** *Epidemiol Infect* 1996;**117:** 457-462.
3. Hoogkamp-Korstanje JAA, Koning de J. **Yersinia enterocolica-infecties; klinische en histologische kenmerken, diagnostiek en therapie**. *Ned Tijdschr Geneeskd* 1991;**135:**nr 47. (Dutch)
4. Loftis AD, Priestly RA, Massung RF. **Detection of Coxiella burnetii in commercially available raw milk from the United States.** *Foodborne Pathog Dis* Dec 2010;7(12)**:**1453-6. Doi:10.1089/fpd.2010.0579. Epub 2010 Aug 12.
5. Langer AJ, Ayers T, Grass J, Lynch J, Angulo FJ, Mahon BE. **Nonpasteurized Dairy Products, Disease Outbreaks, and State Laws – United States, 1993 -2006.** *Emergency Infectious Diseases* 2012;**18**:3.
6. Longenberger AH, Palumbo AJ, Chu AK, Moll ME, Weltman A, Ostroff SM. **Campylobacter jejuni Infections Associated With Unpasteurized Milk – Multiple States, 2012.** *Clinical Infectious Diseases* 2013;**57**(2): 263-6.

Chapter 3

Small risk of developing Lyme borreliosis following a tick bite on Ameland: Research in a general practice

Published in Dutch with original title:

Kleine kans op lymeborreliose na een tekenbeet op Ameland: onderzoek in een huisartsenpraktijk

Jac. J.W.M. Jacobs, Gerda T. Noordhoek, Jon M.M. Brouwers, Peter R. Wielinga, Jan P.A.M. Jacobs and Afke H. Brandenburg

Ned Tijdschr Geneeskd 2008 sept 13;152(37):2022-6

Abstract

Objective. To investigate the percentage of ticks infected with *Borrelia burgdorferi* on the Dutch North Sea island of Ameland, and the risk of developing Lyme disease following tick bite on the island.

Design. Prospective, observational.

Methods. Ticks were collected from patients who visited a general practitioner and then tested for the DNA of *B. burgdorferi*. After 6 months the patients were interviewed by phone using a standardized questionnaire.

Results. Between 2004 and 2006, 216 ticks were collected from 167 patients. Most ticks were removed within 24 hours. *B. burgdorferi* DNA was detected in 44 of the ticks (20.4%). Follow-up information was obtained from 146 patients, 41 (28.1%) them having been bitten by a *Borrelia*-positive tick. None of the patients developed a typical erythema migrans. Of the 13 patients (9%) reporting a non-specific redness of the skin at the site of the tick bite (diameter less than 5 cm), 5 had been bitten by a positive tick and 8 by a negative tick. One patient bit by a positive tick reported systemic symptoms related to Lyme borreliosis, namely fatigue, perspiration and joint ache, without local redness.

Conclusion. The probability of developing Lyme borreliosis was low even though a relatively large percentage of the ticks collected were positive for *B. burgdorferi*. This is probably connected to the fact that in the majority of cases the tick had been removed within 24 hours.

Introduction

In recent years, the general public has become increasingly familiar with Lyme disease, as caused by tick bites, and consultation with as general practitioner has become more frequently. A survey of Dutch general practitioners across a number of years, for example, has shown a doubling of the number of consults for a tick bite and a tripling of the number of diagnoses of "erythema migrans" diagnoses between 1994 and 2005[1]. Other European countries have reported a similar increase in the incidence of Lyme borreliosis[2].

Lyme borreliose is caused by spirochaetes from the *Borrelia burgdorferi*-sensu-latogroup, which contains several distinguishable species (i.e. genospecies). In Europe, infection of humans is caused by three genospecies in particular: *B. burgdorferi sensu stricto*, *B. afzelii* and *B. garini*[3]. Other genospecies are assumed to have no, unclear or minimal pathogenic risk for humans. *B. burgdorferi* is principally transmitted by ticks of the *Ixodes ricinys* species. Contamination with *B. burgdorferi* can occur during all three stages of the life cycle of the tick (i.e., the larva stage, the nymph stage, the adult tick stage), but larva are rarely infected because vertical transmission seldom occurs.

In the Netherlands, the North Sea island of Ameland is often cited as a high-risk environment for tick bite and bite by *B. burgdorferi* ticks in particular. In a 1995 study, *B. burgdorferi*-species DNA was found in 11% of the adult ticks and 23% of the nymphs on the island [4,5]. This observed percentage of contaminated ticks in the region is the reason for the media to regularly warn tourists about the risk of tick bite; to suggest a direct connection between tick bite and the occurrence of Lyme disease; and to therefore prescribe — without empirical foundation or justification — antibiotic prophylaxis for any tick bite. To identify the actual connection (or lack of significant connection) between tick bite and the incidence of Lyme disease on the island of Ameland, we therefore determined the percentage of infected ticks across a given period of time and identified the probability of developing Lyme disease following a tick bite during this same period of time.

Methods

Patients

Between January 2004 and December 2006, ticks from all patients consulting with one or more tick bites at the general practitioner's office in Ballum on Ameland were

collected. Informed consent was obtained from all patients or their parents before removal of the tick and collection of the data needed for the present study. During the first visit, the GP recorded the presence of one or more ticks on the skin and the estimated duration of the attachment of the tick to the skin. The GP also noted whether the patient had tried to remove the tick themselves or not; whether the tick had been completely removed or not; and where on the island the bite was presumed to have taken place. Approximately six months following tick removal the majority of the patients were contacted by telephone by independent interviewer, for the collection of additional data; a few of the patients could only be contacted 12 to 18 months following tick removal. Neither the patient nor the interviewer knew if the tick in a particular case had tested positive or negative for *B. burgdorferi.* During the follow-up telephone interview, information was gathered with regard to whether or not the patient had noticed a red, ring-shaped discoloration of the skin at the site of the tick bite in the weeks following the tick bite and whether or not systemic symptoms presented themselves during the months following the tick bite (i.e., symptoms indicative of lyme borreliose: long lasting fever, symptoms of flu, painful joints, loss of facial musculature, double vision, fainting, cardiac arrhythmia). The patients were also asked if they had visited their own GP for any of the symptoms and, if so, whether they had then been treated with antibiotics for Lyme disease or not. In addition, when the patients indicated that they would like to be informed of whether the tick had been positive or negative for *B. burgdorferi*, they were called back by the GP-researcher on a separate occasion with the results.

Removal of the ticks

The ticks were removed by the GP using special tick tweezers. The tip of the tweezers was positioned as closely as possible to the mouthparts of the tick, and the tick was then extracted with a twisting motion and light pulling. The tick was then placed in a small container with 70% ethanol or in a lysisbuffer (0.5 % natriumdodecylsulfaat; 100 mM Tris-HCl; 10 mM ethyleendiaminetetra-acetic acid; 10 mM NaCl; pH: 8.3; 0.5 mg/ml proteinase K) and sent to the laboratory (Laboratorium voor Volksgezondheid in Friesland), microscopically identified as *Ixodes ricinus* and classified as a larva, nymph or adult tick before being put in a lysis buffer. In the lysis buffer, the ticks were preserved at -20 °C until conduct of the polymerase chain reaction (PCR).

Polymerase chain reaction

In order to detect the presence or absence of *B. burgdorferi* DNA, a raw lysate was created by incubating the tick for one night in a lysis buffer at 55°C. The DNA was

then extracted according to the method described by Boom et al [6]. The PCR was performed with primers specific to the *OspA-gen* of the *B. burgdorferi*[7]. The PCR-product was then analysed in a microwell hybridization assay[8,9], for which a biotin-labeled probe was used, (5'-GACAAGCTTGAGCTTAAAGGAACTTCTG). Determination of the genospecies was performed at the National Institute for Public Health and the Environment (Rijksinstituut voor Volksgezondheid en Milieu; RIVM) in The Netherlands, as described elsewhere[10,11].

Serology

The GP-researcher who communicated the results of the tick bites to the those patients interesting in hearing this six months following the initial consultation for the tick bite asked all of the patients who had been bitten by a tick positive for *B. burgforferi* and some of the patients who had been bitten by a tick negative for the same, if they would be prepared to give some blood for an antibody test. When the patient was willing to cooperate, their blood was tested for antibodies to *B. burgdorferi* in a laboratory located close to the patient's place of residence and according to the laboratory's criteria. In all cases, an ELISA (IgM and IgC or Ig-total) screening test was performed. When a positive screening result was obtained for *B. burgforferi*, a western blot was also then conducted to confirm the result. All results were reported to the researchers.

Statistical analysis

The clinical and epidemiological data for the patients bit by infected versus non-infected ticks were compared using Fischer's exact tests.

Results

Ticks

During the research period 216 ticks were collected from 167 patients; 50 in 2004, 59 in 2005 and 107 in 2006 (Table 1). Of the 167 patients, 42 (25.1 %) were bit by at least 1 positive tick. Of the 216 ticks, 44 (20.4%) were positive for *Borrelia* DNA. The percentage positive ticks remained about the same during the research period (22 in 2004, 18.6 in 2005 and 21 in 2006). Of all the ticks, 33 were in the larva stage and 1 of these was positive (3.0%); 122 were in the nymph stage and 30 of these was positive (24.6%); 52 were in the adult stage and 11 of these positive (21.2 For 9 of the

ticks, the exact stage could not be determined but 2 of these were positive (22.2%). Of the 21 patients who could not be reached for follow-up interview, only 1 (or 5%) has been bitten by a positive tick. This is a significantly lower percentage than for the patients who were reached (5%; p = 0.03 in Fischer's exact test). The data for these two patient groups nevertheless did not differ for the first visit.

The genotype of the positive ticks was determined on the basis of the DNA. In 6 ticks *B. garinii* was found; in 12 *B. afzelii* was found; and in 11 *B. ruski* was found — a genotype only recently described and closely related to *B. afzelii*[12]. *B. burgdorferi sensu stricto* was not found. The genotype of 10 ticks could not be determined due to insufficient Borrelia DNA for correct typification. In 5 ticks, *Borrelia* infection could be confirmed but the genotype could not be determined because the DNA did not match that of the known *Borrelia* genospecies.

Table 1. Number of ticks infected with *Borrelia burgdorferi* in patients consulting at a general practitioner's office on Ameland in the period 2004-2006; data classified according to tick stage

Stage	Number of ticks	Infected; N (%)
Larva	33	1 (3.0)
Nymph	122	30 (24.6)
Adult	52	11 (21.2)
Undefinable	9	2 (22.2)
Total	216	44 (20.4)

Patients

Of the 167 patients, 146 (86.4%) could be reached for a follow-up interview. Of all the interviewed patients, 41 (28.1%) had been bitten by at least one *Borrelia*-positive tick and thus 105 by one or more negative ticks. In the cases of 7 of the 146 patients reached for follow-up, the tick had not been completely removed; in 27 of the cases, the patient had first tried to remove the tick themselves.

Most tick bites were caught in the dunes; the nearby forest was the second highest-ranking place (Table 2). The percentage of positive ticks caught in the dunes did not significantly differ from the percentage caught in the forest ($p = 0.20$ in Fischer's exact test). In most of the cases, the tick was removed from the patient within 24 hours (Table 2).

None of the 146 patients available for follow up reported a typical erythema migrans (Table 2). Only 13 reported a red discoloration of the skin at the site of the tick bite at some point during the first weeks after the tick bite. This red discoloration did not meet the criteria for erythema migrans, however. Of the 13 patients reporting discoloration, 5 had been bitten by a positive tick and 8 by a negative one. The percentage of people reporting redness did not differ significantly for the group bit by a positive versus negative tick ($p = 0.52$ in Fischer's exact test). Remarkable is that 4 of the 5 patients bit by a positive tick subsequently consulted their own general practitioner even though they were not aware of the positive status of the tick. All 4 of these patients were prescribed doxycycline. None of the 8 people bit by a negative tick subsequently consulted with their own physician. In the period following the tick bite, 5 of the 146 patients reported systemic symptoms involving mainly fever, fatigue and muscle ache; 4 of them had been bit by one or more negative ticks. In the case of 1 patient, the tick attachment was for a period of more than 24 hours. This patient reported systemic symptoms at the time after the tick bite, namely fatigue, perspiring and joint ache. This patient tested serologically positive and was therefore treated with doxycycline after initial consultation. This patient was also the only patient showing serologically proven lyme borreliosis following a tick bite in the present study. And on the basis of this information, the percentage of infections following a tick bite was calculated to be 0.7.

Table 2. Epidemiological and clinical characteristics of 146 patients divided into two groups: those bit by a tick positive or negative for DNA of *Borrelia burgdorferi*

Characteristic	Tick negative (n = 105)	Tick positive (n = 41)
Tick caught in		
Dunes	49	22
Forest	37	9
Meadow	2	0
Village	6	2
Unknown	11	8
Estimated duration attachment to body		
< 24 h	87	36
24-48 h	13	4
> 48 h	5	1
Symptoms		
Erythmena migrans	0	0
Redness < 5 cm	8	5
Systemic symptoms	4	1
Treated with doxycycline	0	5

Serology

Serological testing to determine Lyme disease was conducted with 36 patients six months following the tick bite: 29 had been bitten by a positive tick and 7 bitten by a negative tick. The results showed a positive result for 2 of the 29 people who had had a positive tick bite. One of these patients was the aforementioned patient who had shown systemic symptoms but also reported having been bitten by a tick before. The other patient did not report symptoms and the tick was removed within 24 hours but he reported having had several tick bites in the past. In the group of 29 patients who had been bitten by a positive tick, 3 mentioned subsequent redness but the serology was negative. Of the 7 people bit by a negative tick, the serology proved positive for only 1 who had also been bitten by a tick in the past.

Discussion

A relatively high percentage (20.4%) of the tested ticks was found to be positive for *B. burgdorferi*. The percentage was highest for the nymph population (24.6%) and equal to the level reported for Ameland in earlier studies (23% of nymphs testing positive)[4]. While the percentage of infected ticks found by us for Ameland is higher than the 11% and 13% found in studies conducted elsewhere in the Netherlands by the RIVM (National Institute for Public Health and the Environment) [10-13], this percentage is not higher than the average of 23% recently reported for different areas of the Netherlands by researchers from the Wageningen University [14]. The percentage of *Borrelia*-infected ticks in the Netherlands may thus differ regionally and locally with an average ranging from 10% to 20% with Ameland not deviating significantly from this.

Although 42 patients in this study were bit by a tick contaminated with *B. burgdorferi*, only 1 case of actual *Borrelia* infection was detected. It is likely that this low percentage of infection is the result of the quick removal of the tick for most patients. We know from animal testing that the transmission of *B. burgdorferi* rarely occurs when the tick is removed within 24 hours[15,16]. When we conducted serology six months following a tick bite for part of the population of patients who had been bitten in our study, moreover, only 2 cases of Lyme disease were found among 29 patients but the two infected patients reported having had previous tick bites as well: The positive serology can therefore be due to prior infection in these cases. In most of the tested patients, the results were negative — even if they had been bitten by a positive tick. Our serological outcomes thus support the assumption that the chances of transmission of spirochaetes are limited when the tick is removed within 24 hours of attachment.

In our study, 13 patients reported redness where the tick bite had been. In none of the cases did the redness have a diameter of 5 cm or more; the redness also did not meet the criteria for erythema migrans. The number of people reporting redness was also evenly divided across the groups bit by a positive versus negative tick. This occasional redness thus suggests a reaction to the tick bite itself and is in keeping with what we regularly see in general medical practice: occasional redness as a reaction to a tick bite. What we cannot explain is the fact that 4 out of the 5 patients who were bit by a positive tick consulted for redness while none of the 8 patients bit by a negative tick did this. We also cannot rule out the possibility that the redness for at least part of our patients was an atypical sign of early *Borrelia* infection.

A possible shortcoming of the present research is that the patients were interviewed six or more months following the tick bite. We chose to do this in order to be able to assess the symptoms of *Borrelia* infection, which typically manifest themselves after a longer period of time. It is nevertheless possible that patients have forgotten minor symptoms after a period of six or more months.

The percentage of low human *Borrelia* infection following a tick bite identified in the present study is comparable to the percentages of 0.8 to 3.2 identified in other studies from Europe [17-19] and the United States[20-23].

The 2004 Lyme borreliosis guidelines from the CBO (*Centraal Begeleidingsorgaan*; Dutch institute responsible for monitoring the quality of health care in the Netherlands) recommend the prescription of antibiotics only upon clinical symptoms of Lyme borreliosis and not following every tick bite [24]. The redness a-typical of erythema migrans can thus be checked for and monitored. Additional diagnostic screening may be conducted (e.g., PCR on a biopsy or attainment of evidence of seroconversion), but serological follow-up is useless when treatment with antibiotics has already been started, as was the case for 4 of the patients with reported redness in our study; antibody response will fail to occur in the antibiotic treatment of a seronegative patient with erythema migrans[24].

Conclusion

While an average of 20% of the ticks on Ameland are contaminated with *B. burgdoferi*, the chances of actually contracting Lyme disease following a tick bite were shown to be relatively small in the present study: about 1 in 100. This is provided that the tick is removed in time. Our findings thus support treatment guidelines which call for the prescription of antibiotics *only* when clinical symptoms of Lyme borreliosis manifest themselves and *not* following each and every consult for a tick bite.

References

1. Hofhuis A, Giessen JWB van der, Borgsteede FHM, Wielinga PR, Notermans DW, Pelt W van. **Lyme borreliosis in the Netherlands: strong increase in GP consultations and hospital admissions in the past 10 years.** *Euro Surveill* 2006;**11**:E060622.2.

2. Smith R, Takkinen J. **Lyme borreliosis: Europe-wide coordinated surveillance and action needed?** *Euro Surveill* 2006;**11**:E060622.1.

3. Steere AC. **Lyme disease.** *N Engl J Med* 2001;**345**:115-25.

4. Rijpkema S, Nieuwenhuijs J, Franssen FF, Jongejan F. **Infection rates of Borrelia burgdorferi in different instars of Ixodes ricinus ticks from the Dutch North Sea Island of Ameland.** *Exp Appl Acarol* 1994;**18**:531-42.

5. Rijpkema S, Bruinink H. **Detection of Borrelia burgdorferi sensu lato by PCR in questing Ixodes ricinus larvae from the Dutch North Sea island of Ameland.** *Exp Appl Acarol* 1996;**20**:381-5.

6. Boom R, Sol CJA, Salimans MMM, Jansen CL, Wertheim-van Dillen PME, Noorda J van der. **Rapid and simple method for purification of nucleic acids**. *J Clin Microbiol* 1990;**28**:495-503.

7. Demaerschalck I, Ben Messaoud A, de Kesel M, Hoyois B, Lobet Y, Hoet P, et al. **Simultaneous presence of different Borrelia burgdor feri genospecies in biological fluids of Lyme disease patients.** *J Clin Microbiol* 1995;**33**:602-8.

8. Kox LFF, Noordhoek GT, Kunakorn M, Mulder S, Sterrenburg M, Kolk AHJ. **Microwell hybridization assay for detection of PCR products from Mycobacterium tuberculosis complex and the recombinant Mycobacterium smegmatis strain 1008 used as an internal control.** *J Clin Microbiol* 1996;**34**:2117-20.

9. Mansy F, Hoyois B, Vos MJ de, Elsen A van, Bollen A, Godfroid E. **Colorimetric solid-phase capture hybridization assay for detection of amplified Borrelia burgdorferi DNA.** *Biotechniques* 1996;**21**; 122-5.

10. Rijpkema SG, Molkenboer MJ, Schouls LM, Jongejan F, Schellekens JF. **Simultaneous detection and genotyping of three genomic groups of Borrelia burgdorferi sensu lato in Dutch Ixodes ricinus ticks by**

characterization of the amplified intergenic spacer region between 5S and 23S rRNA genes. *J Clin Microbiol* 1995;**33**:3091-5.

11. Wielinga PR, Gaasenbeek C, Fonville M, Boer A de, Vries A de, Dimmers W, et al. **Longitudinal analysis of tick densities and Borrelia, Anaplasma, and Ehrlichia infections of Ixodes ricinus ticks in different habitat areas in the Netherlands.** *Appl Environ Microbiol* 2006;**72**:7594-601.

12. Alekseev AN, Dubinina HV, Pol I van de, Schouls LM. **Identification of Ehrlichia spp. and Borrelia burgdorferi in Ixodes ticks in the Baltic regions of Russia.** J Clin Microbiol 2001;**39**:2237-42.

13. Schouls LM, Pol I van de, Rijpkema SGT, Schot CS. **Detection and identification of Ehrlichia, Borrelia burgdorferi sensu lato, and Bartonella species in Dutch Ixodes ricinus ticks.** *J Clin Microbiol* 1999;**37**:2215-22.

14. Rapport Teken, tekenbeten en Borrelia infecties in Nederland. Periode juli-december 2006. De Natuurkalender. Wageningen: Universiteit Wageningen; 2006 . (Dutch)

15. Piesman J, Maupin GO, Campos EG, Happ CM. **Duration of adult female Ixodes dammini attachment and transmission of Borrelia burgdorferi, with description of needle aspiration isolation method.** *J Infect Dis* 1991;**163**:895-7.

16. Piesman J, Mather TN, Sinsky RJ, Spielman A. **Duration of tick attachment and Borrelia burgdorferi transmission.** *J Clin Microbiol* 1987;**25**:557-8.

17. Maiwald M, Oehme R, March O, Petney TN, Kimmig P, Naser K, et al. **Transmission risk of Borrelia burgdorferi sensu lato from Ixodes ricinus ticks to humans in southwest Germany.** *Epidemiol Infect* 1998;**121**:103-8.

18. Nahimana I, Gern L, Blanc DS, Praz G, Francioli P, Péter O. **Risk of Borrelia burgdorferi infection in western Switzerland following a tick bite.** *Eur J Clin Microbiol Infect Dis* 2004;**23**:603-8.

19. Merino FJ, Nebreda T, Serrano JL, Fernández-Soto P, Encinas A, Pérez-Sánchez R. **Tick species and tick-borne infections identified in**

population from a rural area of Spain. *Epidemiol Infect* 2005;**133**:943-9.

20. Nadelman RB, Nowakowski J, Fish D, Falco RC, Freeman K, McKenna D, et al. **Prophylaxis with single-dose doxycycline for the prevention of Lyme disease after an Ixodes scapularis tick bite. Tick Bite Study Group.** *N Engl J Med* 2001;**345**:79-84.

21. Shapiro ED, Gerber MA, Holabird NB, Berg AT, Feder jr HM, Bell GL, et al. **A controlled trial of antimicrobial prophylaxis for Lyme disease after deer-tick bites.** *N Engl J Med* 1992;**327**:1769-73.

22. Costello CM, Steere AC, Pinkerton RE, Feder jr HM. **A prospective study of tick bites in an endemic area for Lyme disease.** *J Infect Dis* 1989;**159**:136-9.

23. Agre F, Schwartz R. **The value of early treatment of deer tick bites for the prevention of Lyme disease.** *Am J Dis Child* 1993;**147**:945-7.

24. Richtlijn Lyme-borreliose. Utrecht: Kwaliteitsinstituut voor de Gezondheidszorg CBO; 2004. (Dutch)

Chapter 4

Small risk of developing symptomatic tick-borne diseases following a tick bite in the Netherlands

Ellen Tijsse-Klasen, Jac J.W.M. Jacobs, Manoj Fonville, Johan H. Reimerink, Afke H. Brandenburg, Joke W. B. van der Giessen, Agnetha Hofhuis, Arno Swart and Hein Sprong, *Parasites & Vectors 2011, **4:**17doi:10.1186/1756-3305-4-17*

Abstract
In The Netherlands, the incidence of Lyme borreliosis is on the rise. Besides its causative agent, *Borrelia burgdorferi* s.l., other potential pathogens like *Rickettsia*, *Babesia* and *Ehrlichia* species are present in *Ixodes ricinus* ticks. The risk of disease associated with these microorganisms after tick-bites remains, however, largely unclear. A prospective study was performed to investigate how many persons with tick-bites develop localized or systemic symptoms and whether these are associated with tick-borne microorganisms. In total, 297 *Ixodes ricinus* ticks were collected from 246 study participants who consulted a general practitioner on the island of Ameland for tick bites. Ticks were subjected to PCR to detect DNA of *Borrelia burgdorferi s.l.*, *Rickettsia* spp., *Babesia* spp. or *Ehrlichia/Anaplasma* spp.. Sixteen percent of the collected ticks were positive for *Borrelia burgdorferi s.l.*, 19% for *Rickettsia* spp., 12% for *Ehrlichia/Anaplasma* spp. and 10% for *Babesia* spp. At least six months after the tick bite, study participants were interviewed on symptoms by means of a standard questionnaire. 14 out of 193 participants (8.3%) reported reddening at the bite site and 6 participants (4.1%) reported systemic symptoms. No association between symptoms and tick-borne microorganisms was found. Attachment duration ≥24h was positively associated with reddening at the bite site and systemic symptoms. Using logistic regression techniques, reddening was positively correlated with presence of *B. burgdorferi afzelii*, and having 'any symptoms' was positively associated with attachment duration. The risk of contracting Lyme borreliosis, rickettsiosis, babesiosis or ehrlichiosis from a single tick bite was <1% in this study population.

Introduction

The most prevalent and widespread vector-borne disease of humans and animals in the northern hemisphere is Lyme borreliosis. Early detection of Lyme borreliosis is crucial, as antibiotics are most effective at this stage, preventing the development of later, more severe stages of the disease [1]. Over the last decade, the incidence of Lyme borreliosis has increased significantly in Europe, with up to 16 and 21 cases per 10,000 individuals reported in Scandinavia and Slovenia, respectively [2]. A periodical retrospective study under general practitioners in The Netherlands has shown a continuing and strong increase in general practitioner (GP) consultations for erythema migrans and hospital admissions in the past 15 years with 22000 cases in 2009. The most straightforward explanation for this increase is the concomitant increase in the number of GP consultations for tick bites [3,4]. Although direct evidence is lacking, the factors responsible for this increase are most probably a combination of higher tick numbers and intensified human recreational behaviour, leading to an increased exposure of the population to tick bites.

The same tick species transmitting the etiologic agents of Lyme disease in Europe, *Ixodes ricinus*, also serves as vector of pathogens causing tick-borne encephalitis, babesiosis, several forms of rickettsioses and anaplasmoses. Incidences and public health risks of tickborne diseases other than Lyme borreliosis are largely unknown in The Netherlands, but also in other countries. Although Dutch ticks have been shown to have a high prevalence of *Rickettsia helvetica* and can contain *Babesia,* so far no endemic disease cases in humans have been observed for these microorganisms [5,6]. *R. helvetica* is a intracellular bacterium that is suspected of causing acute perimyocarditis, unexplained febrile illness and sarcoidosis[7-12]. Various *Babesia* species are known to cause disease in humans and animals with *Babesia divergens* being the most important human pathogenic species in Europe[6]. *Anaplasma* and *Ehrlichia* have also been found in Dutch ticks and a few human cases have been reported in the Netherlands [13,14]. Not only transmitted pathogens but also the tick itself can lead to health impairments. Ticks secrete a complex mixture of bio-active compounds, mainly proteins, during the blood meal[15-17]. These can have local or systemic toxic effects or induce an immune response.

Individuals rarely react with intense anaphylaxis but milder allergic reactions are probably more common and easily overlooked[18-20].The risk of developing Lyme borreliosis or any other tick-borne disease after a tick bite depends on many unrelated factors, including the tick species, the infection rate of the tick, the site and duration of the tick bite, the (genetic) constitution of the pathogen and its potential

host[21-23]. Many, if not all, of these factors may vary geographically and in time. Several prospective studies have estimated the risk of developing Lyme borreliosis following a tick bite, but not in The Netherlands, and rarely for other tick-borne diseases such as spotted fever rickettsiosis, babesiosis, and anaplasmosis [24-27]. Data on Borrelia infection on patients and ticks from the years 2004-2006 were previously reported [28]. Field studies between 1989 and 1993 on the Dutch island of Ameland reported a *B. burgdorferi* prevalence in ticks (n=463) of 25% (95% CI: 21-29%)[29,30], which led to an increased awareness of Lyme disease on the island. To estimate the risk of developing symptoms following tick bites and to investigate whether this risk is associated to specific tickborne pathogens a study was initiated. Patients who consulted one GP on Ameland for a tick bite were to participate. They were asked to fill out a questionnaire on the day they visited the GP and were approached again several months later. The ticks were tested for *Borrelia burgdorferi s.l., Rickettsia* spp.*, Babesia* spp. and *Ehrlichia/Anaplasma* spp..

Material and Methods

Study participants

Between January 2004 and December 2008 ticks were collected from patients with one or more tick bites that consulted the GP in the village of Ballum on Ameland (53°44'41N, 5°68'43E). Ballum is the smallest village on Ameland with only about 370 citizens but about 500000 tourists visit this village yearly. This is represented in the composition of the study population of which only 20 % was a resident of the island. Patients or their guardians were asked for an informed consent for testing the tick for various microorganisms and for collecting data via questionnaires or interviews. In a first questionnaire data were collected concerning, amongst others, the number of tick bites and duration of tick attachment. Approximately six months after the first visit to the GP patients were contacted by phone and interviewed. Some of the patients where only reached after 12 to 18 months. This second interview aimed at identifying possible symptoms related to the tick bite including local redness or erythema migrans and systemic symptoms as fever, malaise, palpitations, joint problems, or neurological symptoms, and if so whether they consulted a GP for this symptoms.

Removal and analysis of ticks

Ticks were carefully removed by the general practitioner and were immersed in 70% ethanolor a lysis buffer (0,5% sodium dodecyl sulfate; 100 mM tris-(hydroxymethyl) aminomethane; 10 mM ethylenediaminetetraacetic acid; 10 mM NaCl; pH: 8,3; 0,5 mg/ml protease K) and sent to the laboratory. Ticks stored in ethanol were determined to species level and DNA was extracted as described earlier [28]. Tick DNA extracts were analyzed by polymerase chain reaction (PCR) followed by reverse line blotting (RLB), as described elsewhere [31]. Primers and probes are described in Table 1.

Statistics

Outcomes were defined as redness on the site of the tick bite, and/or any systemic symptoms such as fever, malaise or pain. Risk factors that were investigated included positive PCR/RLB results for one of the micro-organisms (*Borrelia*, *Rickettsia*, *Babesia* or *Ehrlichia*/*Anaplasma*) in the ticks, any of these (= any micro-organism), duration (<24h, between 24h and 48h, >48h) and number of tick bites.

Firstly, we tested for all possible outcomes - risk factor combinations, the strength of association (null hypothesis of unity odds ratio, i.e. no association). To this end, contingency tables were constructed and Fisher's exact tests were performed for each combination. All calculations were performed using R 2.11.1, using the 'Epi' package v1.1.17. For outcomes and binary risk factors (i.e. absence-presence of microorganisms), risk ratios and their 95% confidence intervals were computed. For non-binary risk factors categories were defined. Furthermore we calculated the exact p-value for the hypothesis of unity odds-ratio. The results are presented in tables 2-4.

For purposes of logistic regression, it is convenient to know what factors are associated at the70% significance level [32]. Fisher's exact test outcomes were significant ($p<0.30$) at this level for local redness with attachment duration of more than 24h, more than 48h, more than two tick bites and *B. burgdorferi afzelii*, for systemic symptoms with >24h, *Ehrlichia* spp. and *B. garinii* infection of the tick and for any symptom with >24h, >48h, any infection of the tick, *B.burgdorferi afzelii* and *Borrelia burgdorferi s.l.*. These factors and categorical data (number of bites, number of days the tick was attached) were included in backwards logistic regressions for each outcome variable. Any combination of microorganism and days of attachment was also tested in the logistic regression.

Results

Ticks were collected from 246 study participants. In total 297 ticks were removed ranging from 1 to 18 ticks per individual with an average of 1.2 ticks per individual. All ticks that were identified to species level were *Ixodes ricinus*. Life stages of 236 ticks could be determined microscopically. Of these ticks, 65 (28%) were adults, 133 (56%) were nymphs and 38 (16%) were larvae. Two hundred-ninety-four ticks were tested for *Borrelia burgdorferi s.l., Rickettsia* spp. and *Babesia* spp., 286 ticks were also tested for *Ehrlichia/Anaplasma* spp.. One hundred-ninety-three (78.5%) participants were reached for a second interview, 51 participants were lost to follow-up. For epidemiological analysis only data of the responding participants were used.Of all tested ticks 58% were negative for all microorganisms tested for. 16% were positive for *B. burgdorferi s.l.*, 19% for *Rickettsia* spp., 10% for *Babesia* spp. and 12% for *Ehrlichia/Anaplasma* spp.. The overall infection rate with *B. burgdorferi* s.l. was 16% (n=294, CI 12.1-21.1%), which is significantly lower (p= 0.005) than in the early 1990s (25% (n=463, CI20.5-28.9%; ref) [29]. Different sub-species of *B. burdorferi* s.l. were found during this study of which *B. burgdorferi afzelii* was the most common one. *Rickettsiae* that were identified to species level were *Rickettsia helvetica* and *Rickettsia monacensis*. Infection rates of the different life stages were calculated and are presented in figure 1. No larvae were found positive for *Babesia* and only one for *Borrelia*.

In total 22 study participants reported symptoms of which 14 reported reddening around the tick bite site and 6 reported systemic symptoms and 2 reported both. This corresponds to an absolute risk of 11.4% for developing symptoms and 8.3% and 4.1%, respectively, for local reddening and systemic symptoms after a tick bite. 171 participants reported no symptoms. Reddening at the bite site did not show the pattern of erythema migrans in any of the cases. Systemic symptoms included fever (n=3), malaise (n=3), fatigue (n=3), panic attacks (n=1), muscle pain (n=1), joint pain (n=1) or stiffness of the neck (n=1). Three study participants reported symptoms but did not specify them further. Eighty-four percent of the participants reported that the tick had been attached less than 24 hours while 4.7% reported that the tick had been attached for more than 48 hours. The occurrence of symptoms or reddening at the bite site was not correlated with the infectious state of the ticks (table 2, 3, 4). However, a significant positive correlation (at 95% significance) was found between attachment duration of ticks (≥24h) and symptoms. This was the case for redness (p = 0.08) and systemic symptoms (p = 0.02) analyzed individually and also when symptoms were analyzed conjointly (p= 0.009).

The logistic regression yielded no significant result for systemic symptoms. For redness, or any symptoms the following significant regression was found,

$$R = \quad e^{0.79d}\, e^{1.1A} / 36.6 + e^{0.79d}\, e^{1.1A}$$

$$G = \quad e^{0.8d} / 21.8 + e^{0.8d}$$

where R is the probability of redness at d days of tick presence and A indicates absence ('0' or presence ('1') of *B. burgdorferi afzelii*. G is the probability of systemic symptoms depending again on the number of days d. Logistic regression indicated the presence of one *B. burgdorferi* sub-species, *B. burgdorferi afzelii*, to be associated with local reddening. For example, 4 days of *B. burgdorferi afzelii* presence yields a probability of redness of 66%.

Discussion

Tick bites may cause serious and lasting effects due to transmitted pathogens. Symptoms, especially localized ones, can also be due to reaction towards the tick itself. During this study several risk factors for developing localized and systemic symptoms were investigated. Ticks were tested for four different groups of micro-organsims. Statistical analysis showed none of the micro-organsims to be significantly associated to systemic symptoms but logistic regression indicated that *B. burgdorferi afzelii* might be associated with local reddening. Tick attachment duration was found to be strongly associated with an increased risk for developing localized reddening at the bite site as well as systemic symptoms. This association is most probably due to a direct response towards the tick or substances it secreted into the wound. Ticks secrete a complex mixture of compounds, some of which are potentially toxic, and which accumulate during the feeding process. Castelli *et al.*[33] described local reactions as result of tick bites. These included nodules, erythema and alopethia. Severe systemic symptoms can also follow a tick bite. One example is tick paralysis which has been reported from patients mainly in North America and Australia. Several tick species have been associated with this disease including some *Ixodes* species [34]. *I. ricinus*, however, has so far not been associated with tick paralysis. A longer attachment period is likely to increase the risk of developing localized or systemic symptoms due to excreted tick proteins and also due to pathogens [35]. Timely removal of a tick is therefore a major factor to reduce transmission of potentially toxic tick excretions and tick-borne pathogens and our study supports that it significantly lowers the risk of developing symptoms.

Prevalence of *Borrelia burgdorferi s.l.*, *Babesia* spp. and *Ehrlichia/Anaplasma* spp. in ticks collected during this study was lower in larvae than in adult ticks. This indicates that these microorganisms need vertebrate hosts to maintain themselves in the tick populations. However, transovarial transmission seems to play a minor role for *Ehrlichia/Anaplasma* and a major role for *Rickettsia* spp. as the prevalence of these bacteria in larvae was already 8.1% and 26%, respectively. For *Rickettsia* spp. the prevalence was similar in adults, nymphs and larvae. This was observed in an earlier study as well and indicates that *Rickettsiae* are transmitted transovarially at a high degree and therefore do not rely on a vertebrate host [5].

A remarkable observation is that the prevalence of *B. burgdorferi s.l.* in ticks decreased significantly from 1989/1993 to 2004/2008. This seems to contradict findings that Lyme disease is on the rise in the Netherlands[3,4]. However, an increase in disease incidence is more likely due to an increased exposure of people to infected ticks. This can also be caused by a change in recreational behaviour or in the number of ticks present in the environment. Although these factors are difficult to measure and have not been measured during this study it seems likely that these and not an increase in infection rate are responsible for an increase in disease incidence.

Conclusion

In our study, the overall risk of developing symptoms after a tick bite is 11.4% and most of these symptoms are restricteId to local reactions. The risk of contracting symptoms of Lyme borreliosis after a single tick bite, even if the tick is infested with potential pathogens, is lower than 1%. Based upon the data collected in this study none of the participants developed symptomatic Rickettsiosis, Babesiosis or Ehrlichiosis. This means that the risk of contracting overt symptoms one of these diseases was lower than 0.5% in this study population. The study shows that prompt removal of ticks reduces the risk of developing symptoms after a tick bite. Thorough checking for ticks together with appropriate clothing, tick avoiding behavior and use of insect repellents, is therefore the most powerful measure to prevent tick-borne diseases.

Acknowledgements

We thank Wilfrid van Pelt for critically reading the manuscript and his advice on data analysis. This study was financially supported by the Dutch Food and Consumer Product Safety Authority (VWA) and by the Ministry of Health, Welfare and Sport.

References

1. Girschick HJ, Morbach H, Tappe D. **Treatment of Lyme borreliosis.** *Arthritis ResTher* 2009,**11**:258.
2. Smith R, Takkinen J. **Lyme borreliosis. Europe-wide coordinated surveillance and action needed?** *Euro Surveill* 2006,**11:**E060622.1.
3. Hofhuis A, Giessen Jvd, Borgsteede F, Wielinga P, Notermans D, Pelt W van. **Lyme borreliosis in the Netherlands: strong increase in GP consultations and hospitaladmissions in past 10 years.** *Euro Surveill* 2006,**11:**E060622.2.
4. Hofhuis A, Harms MG, Giessen JWBvd, Sprong H, Notermans DW, Pelt W van: **Ziekte van Lyme in Nederland 1994-2009: Aantal huisartsconsulten blijft toenemen. Is voorlichting en curatief beleid genoeg?** *Infectieziekten Bulletin* 2010, **21** (Dutch).
5. Sprong H, Wielinga PR, Fonville M, Reusken C, Brandenburg AH, Borgsteede F, Gaasenbeek C, van der Giessen JW. **Ixodes ricinus ticks are reservoir hosts for Rickettsia helvetica and potentially carry flea-borne Rickettsia species.** *Parasit Vectors* 2009;**2**:41.
6. Kjemtrup AM, Conrad PA. **Human babesiosis: an emerging tick-borne disease.** *Int J Parasitol* 2000;**30**:1323-1337.
7. Nielsen H, Fournier PE, Pedersen IS, Krarup H, Ejlertsen T, Raoult D. **Serologicaland molecular evidence of Rickettsia helvetica in Denmark.** *Scand J Infect Dis* 2004;**36**:559-563.
8. Fournier PE, Allombert C, Supputamongkol Y, Caruso G, Brouqui P, Raoult D. **Aneruptive fever associated with antibodies to Rickettsia helvetica in Europe and Thailand.** *J Clin Microbiol* 2004;**42**:816-818.
9. Nilsson K. **Septicaemia with Rickettsia helvetica in a patient with acute febrile illness, rash and myasthenia.** *J Infect* 2008.
10. Nilsson K, Lindquist O, Pahlson C. **Association of Rickettsia helvetica with chronic perimyocarditis in sudden cardiac death.** *Lancet* 1999;**354**:1169-1173.
11. Cinco M, Luzzati R, Mascioli M, Floris R, Brouqui P. **Serological evidence ofRickettsia infections in forestry rangers in north-eastern Italy.** *Clin Microbiol Infect* 2006;**12**:493-495.
12. Nilsson K, Pahlson C, Lukinius A, Eriksson L, Nilsson L, Lindquist O. **Presence of Rickettsia helvetica in granulomatous tissue from patients with sarcoidosis.** *J Infect Dis* 2002;**185**:1128-1138.

13. Doudier B, Olano J, Parola P, Brouqui P. **Factors contributing to emergence of Ehrlichia and Anaplasma spp. as human pathogens.** *Vet Parasitol* 2010;**167**:149-154.
14. van Dobbenburgh A, van Dam AP, Fikrig E. **Human granulocytic ehrlichiosis in western Europe.** *N Engl J Med* 1999;**340**:1214-1216.
15. Valenzuela JG. **Exploring tick saliva: from biochemistry to 'sialomes' and functional genomics.** *Parasitology* 2004,**129**:S83-94.
16. Steen NA, Barker SC, Alewood PF. **Proteins in the saliva of the Ixodida (ticks): pharmacological features and biological significance.** *Toxicon* 2006;**47**:1-20.
17. Francischetti IM, Sa-Nunes A, Mans BJ, Santos IM, Ribeiro JM. **The role of saliva in tick feeding.** *Front Biosci* 2009,**14**:2051-2088.
18. Fernandez-Soto P, Davila I, Laffond E, Lorente F, Encinas-Grandes A, Perez-Sanchez R. **Tick-bite-induced anaphylaxis in Spain**. *Ann Trop Med Parasitol* 2001; **95**:97-103.
19. Acero S, Blanco R, Bartolome B. **Anaphylaxis due to a tick bite**. *Allergy* 2003, **58**:824-825.
20. Beaudouin E, Kanny G, Guerin B, Guerin L, Plenat F, Moneret-Vautrin DA. **Unusual manifestations of hypersensitivity after a tick bite: report of two cases.** *Ann Allergy Asthma Immunol* 1997,**79**:43-46.
21. Lane RS, Piesman J, Burgdorfer W. **Lyme borreliosis relation of its causativeagent to its vectors and hosts in North America and Europe.** *Annu Rev Entomol* 1991;**36**:587-609.
22. Piesman J, Mather TN, Sinsky RJ, Spielman A. **Duration of tick attachment and Borrelia burgdorferi transmission.** *J Clin Microbiol* 1987;**25**:557-558.
23. Wang G, Ojaimi C, Wu H, Saksenberg V, Iyer R, Liveris D, McClain SA, Wormser GP, Schwartz I. **Disease severity in a murine model of lyme borreliosis is associated with the genotype of the infecting Borrelia burgdorferi sensu stricto strain.** *J Infect Dis* 2002;**186**:782-791.
24. Sood SK, Salzman MB, Johnson BJ, Happ CM, Feig K, Carmody L, Rubin LG, Hilton E, Piesman J**. Duration of tick attachment as a predictor of the risk of Lyme disease in an area in which Lyme disease is endemic.** *J Infect Dis* 1997;**175**:996-999.
25. Costello CM, Steere AC, Pinkerton RE, Feder HM, Jr. **A prospective study of tick bites in an endemic area for Lyme disease.** *Conn Med* 1989;**53**:338-340.

26. Nilsson K, Lukinius A, Pahlson C, Moron C, Hajem N, Olsson B, Lindquist O. **Evidence of Rickettsia spp. infection in Sweden: a clinical, ultrastructural and serological study.** *Apmis* 2005;**113**:126-134.
27. Bjoersdorff A, Wittesjo B, Berglun J, Massung RF, Eliasson I. **Human granulocytic ehrlichiosis as a common cause of tick-associated fever in Southeast Sweden: report from a prospective clinical study.** *Scand J Infect Dis* 2002;**34**:187-191.
28. Jacobs JJWM, Noordhoek GT, Brouwers JMM, Wielinga PR, Jacobs JPAM, Brandenburg AH: **[Small risk of developing Lyme borreliosis following a tick bite on Ameland: research in a general practice].** *Ned Tijdschr Geneeskd* 2008;**152**(37):2022-2026. (Dutch)
29. Rijpkema S, Nieuwenhuijs J, Franssen FF, Jongejan F. **Infection rates of Borrelia burgdorferi in different instars of Ixodes ricinus ticks from the Dutch North Sea Island of Ameland.** *Exp Appl Acarol* 1994;**18**:531-542.
30. Jongejan F, Rijpkema S. **[Borrelia burgdorferi from Ixodes ricinus ticks on Ameland].** *Tijdschr Diergeneeskd* 1989;**114**:1195-1197. (Dutch)
31. Tijsse-Klasen E, Fonville M, Reimerink JH, Spitzen-van der Sluijs A, Sprong H. **Role of sand lizards in the ecology of Lyme and other tick-borne diseases in the Netherlands.** *Parasit Vectors* 2010;**3**:42.
32. Dohoo I, Martin W, Stryhn H. *Veterinary Epidemiological Research*. Charlottetown: AVC Inc.; 2007.
33. Castelli E, Caputo V, Morello V, Tomasino RM. **Local reactions to tick bites.** *Am J Dermatopathol* 2008;**30**:241-248.
34. Vedanarayanan V, Sorey WH, Subramony SH. **Tick paralysis.** *Semin Neurol* 2004;**24**:181-184.
35. Dana AN. **Diagnosis and treatment of tick infestation and tick-borne diseases with cutaneous manifestations.** *Dermatol Ther* 2009;**22**:293-326.

Table 1. Primers and probes used in this study for PCR and RLB.

Name	Sequence (5' - 3')	Type	Target	Species	Reference
5S borSeq	GAGTTCGCGGGAGAGTAGGTTATTGCC [(1)]	Primer	23S-5S IGS	*B. burgdorferi* sensu lato	[38]
23S borSeq	TCAGGGTACTTAGATGGTTCACTTCC	Primer	23S-5S IGS	*B. burgdorferi* sensu lato	[38]
A-borsl1	CTTTGACCATATTTTTATCTTCCA	Probe	23S-5S IGS	*B. burgdorferi* sensu lato	[39]
A-borsl2	CTTCCATCTCTATTTAGCCAATTT	Probe	23S-5S IGS	*B. burgdorferi* sensu lato	[38]
A-borsl3	TATTTTTATCTTCCATCTCTATTTT	Probe	23S-5S IGS	*B. burgdorferi* sensu lato	[38]
B31-A-s.stricto	AACACCAATATTTAAAAAACATAA	Probe	23S-5S IGS	*B. burgdorferi* sensu stricto	[39]
Ga2-garinii	AACATGAACATCTAAAAACATAAA	Probe	23S-5S IGS	*B. garinii*	[39]
Vs46lN2afzelii	AACATTTAAAAAATAAATTCAAGG	Probe	23S-5S IGS	*B. afzelii*	[39]
VsII62 val	CATTAAAAAAATATAAAAAATAAATTTAAGG	Probe	23S-5S IGS	*B. valaisiana*	[39]
A-Ruski	GAATAAAACATTCAAATAATATAAAC	Probe	23S-5S IGS	*B. afzelii (variant ruski)*	[40]
A-LusiP	CAAAAAAATGAACATTTAAAAAC	Probe	23S-5S IGS	*B. lusitaniae*	[41]
B-GA1b	CGGGATCCCGAGTTTGCCGGGACTTCTTCT [(1)]	Primer	*16SrRNA*	*Ehrlichia/Anaplasma*	[42]
16S8Fe	GGAATTCAGAGTTGGATCMTGGYTCAG	Primer	*16SrRNA*	*Eubacteria*	[43]
Ehr-all	TTATCGCTATTAGATGAGCC	Probe	*16SrRNA*	*Anaplasma* genus	[42]
A-HGE	GCTATAAAGAATAGTTAGTGG	Probe	*16SrRNA*	HGE agent	[42]
A-Eqph	TTGCTATAAAGAATAATTAGTGG	Probe	*16SrRNA*	*A. phagocytophilum*	[42]

Name	Sequence (5' - 3')	Type	Target	Species	Reference
A-dHGE	GCTATGAAGAATAGTTAGTG	Probe	*16SrRNA*	HGE agent (variant)	[42]
A-dPh	TTGCTATGAAGAATAATTAGT	Probe	*16SrRNA*	*A. phagocytophilum variant*	[38]
A-E.Schot	GCTGTAGTTTACTATGGGTA	Probe	*16SrRNA*	*A. schotti* (variant)	[42]
A-murisT	AGCTATAGGTTTGCTATTAGT	Probe	*16SrRNA*	*E. muris* T variant	[40]
A-Chaff	ACCTTTTGGTTATAAATAATTGTTA	Probe	*16SrRNA*	*E. chaffeensis*	[42]
A-can	TCTGGCTATAGGAAATTGTTA	Probe	*16SrRNA*	*E. canis*	[42]
A-Wolbach	CTACCAAGGCAATGATCTA	Probe	*16SrRNA*	*Wolbachia*	[38]
Rick-16S rev	ACTCACTCGGTATTGCTGGA [(1)]	Primer	*16SrRNA*	*Rickettsia* genus	[41]
Rick-16S for	AACGCTATCGGTATGCTTAACA	Primer	*16SrRNA*	*Rickettsia* genus	[41]
A-Rickall	TTTAGAAATAAAAGCTAATACCG	Probe	*16SrRNA*	*Rickettsia* genus	[41]
A-Rhelv2	GCTAATACCATATATTCTCTATG	Probe	*16SrRNA*	*R. helvetica*	[41]
A-Rconor	CTTGCTCCAGTTAGTTAGT	Probe	*16SrRNA*	*R. conorii*	[41]
A-16SRickIRS	GTATATTCTCTACGGAAAAAA	Probe	*16SrRNA*	*Rickettsia* IRS3	[41]
A-RProwaz	CGGATTAACTAGAGCTCGCT	Probe	*16SrRNA*	*Rickettsia prowazekii*	[34]
A-RTyphi	CGGATTAATTAGAGCTTGCT	Probe	*16SrRNA*	*Rickettsia typhi*	[34]
A-NonHelv A	AATACCGTATATTCTCTACGGA	Probe	*16SrRNA*	Non- *Rickettsia helvetica*	[34]
A-NonHelv B	AATACCGTATATTCTCTGCGGA	Probe	*16SrRNA*	Non- *Rickettsia helvetica*	[34]
BATH-Rn	TAAGAATTTCACCTCTGACAGTTA [(1)]	Primer	*18SrRNA*	*Babesia* genus	[44]
BATH-Fn	ACACAGGGAGGTAGTGACAAG	Primer	*18SrRNA*	*Babesia* genus	[44]
Catch all 2	GTAATGGTTAATAGGARCRGTT	Probe	*18SrRNA*	*Babesia* genus	[44]
Ba-div	GTTAATATTGACTAATGTCGAG	Probe	*18SrRNA*	*B. divergens*	[45]
Ba-mic 1	CCGAACGTTATTTTATTGATTT	Probe	*18SrRNA*	*B. microti*	[34]
Ba-mot	GCTTGCTTTTTTGTTACTTTG	Probe	*18SrRNA*	*B. motasi*	[44]
Ba-mic 2	GRCTTGGCATCWTCTGGA	Probe	*18SrRNA*	*B. microti*	[44]
Ba-EU1	CTGCGTTATCGAGTTATTG	Probe	*18SrRNA*	*B. EU1*	[34]

Probes were 5'-amino-labeled. [(1)] Reverse primer 5'-labeled with biotine tetraethyleneglycol

Table 2. Different tick-borne microorganisms found in ticks collected from humans.

Species	positive ticks
Borrelia burgdorferi s.l.	47/297
B. afzelii	33
B. garinii	6
B. valaisiana	1
undetermined	7
Rickettsia spp.*	55/297
R. helvetica	40
R. monacensis	11
undetermined	5
Ehrlichia/Anaplasma spp.	33/289
Ehrlichia sp. schotti variant	31
A. phagocytophilum	1
undetermined	1
Babesia spp.	28/297
B. microti	27
undetermined	1

Microorganisms in tick lysates were detected and identified by PCR followed by RLB.
One tick had a double infection with *R. helvetica* and *R. monacensis*

Table 3. Relative risks of developing any symptom correlated to various risk factors.

	Exposed individuals	Any symptom	Relative risk (95% CI)	P value
>24 h	30/193	8/30	3.10 (1.43 - 6.75)	0.0092*
Borrelia	43/190	7/43	1.60 (0.70 - 3.66)	0.2841
Rickettsia	41/190	6/41	1.36 (0.57 - 3.26)	0.5809
Ehrlichia	27/182	4/27	1.44 (0.52 - 3.97)	0.5059
Babesia	26/190	2/26	0.63 (0.16 - 2.54)	0.7439
Any infection	98/190	14/98	1.64 (0.72 - 3.73)	0.2625

Relative risks were calculated by dividing incidence rates of exposed by incidence rates of unexposed participants. Confidence intervals and p-values were calculated using Fisher's exact test. P-values below 0.05 (*) were regarded as significant.

Table 4. Relative risks of developing redness at the bite site correlated to various risk factors.

	Exposed individuals	Redness on bite site	Relative risk (95% CI)	P value
>24 h	30/193	5/30	2.47 (0.92 - 6.60)	0.0801
Borrelia	43/190	5/43	1.55 (0.57 - 4.22)	0.3647
Rickettsia	41/190	3/41	0.84 (0.25 - 2.80)	1
Ehrlichia	27/182	2/27	0.96 (0.23 - 4.04)	1
Babesia	26/190	2/26	0.90 (0.22 - 3.74)	1
Any infection	98/190	10/98	1.56 (0.59 - 4.13)	0.4382

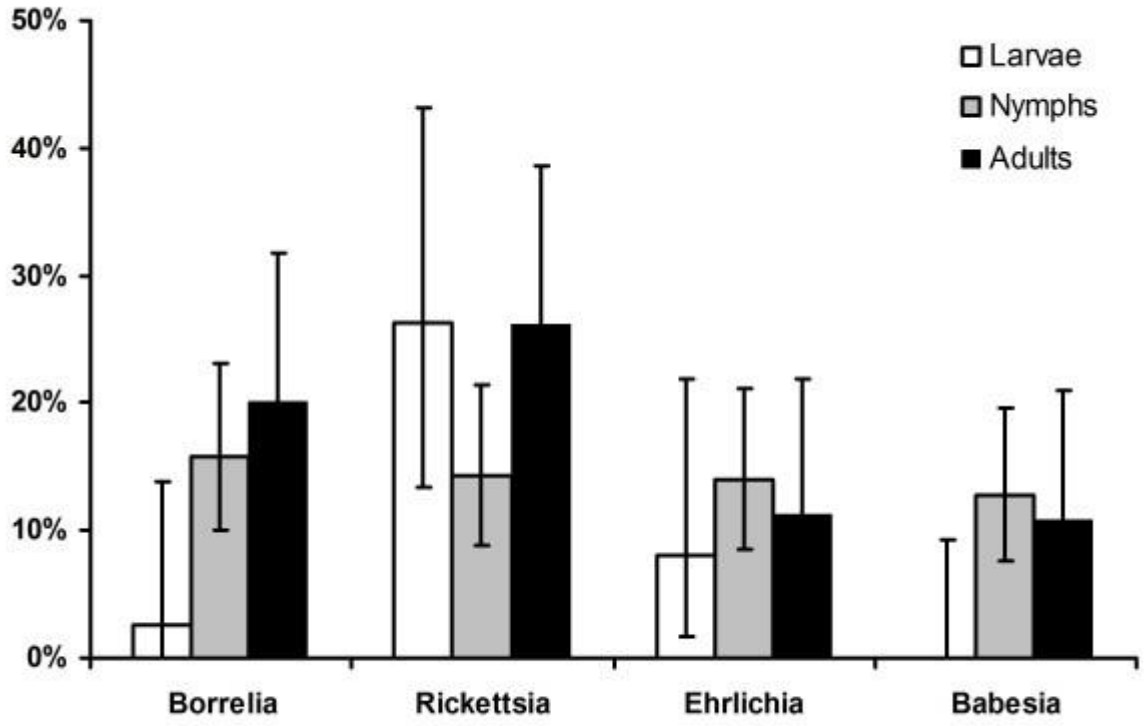
Relative risks were calculated by dividing incidence rates of exposed by incidence rates of unexposed participants. Confidence intervals and p-values were calculated using Fisher's exact test. P-values below 0.05 (*) were regarded as significant.

Table 5. Relative risks of developing systemic symptoms correlated to various risk factors.

	Exposed individuals	Systemic symptoms	Relative risk (95% CI)	P value
>24 h	30/193	4/30	5.43 (1.44 - 20.54)*	0.0215*
Borrelia	43/190	2/43	1.14 (0.24 - 5.44)	1
Rickettsia	41/190	3/41	2.18 (0.54 - 8.75)	0.3729
Ehrlichia	27/182	2/27	2.30 (0.47 - 11.24)	0.2779
Babesia	26/190	1/26	0.90 (0.12 - 7.03)	1
Any infection	98/190	5/98	1.56 (0.38 - 6.36)	0.7218

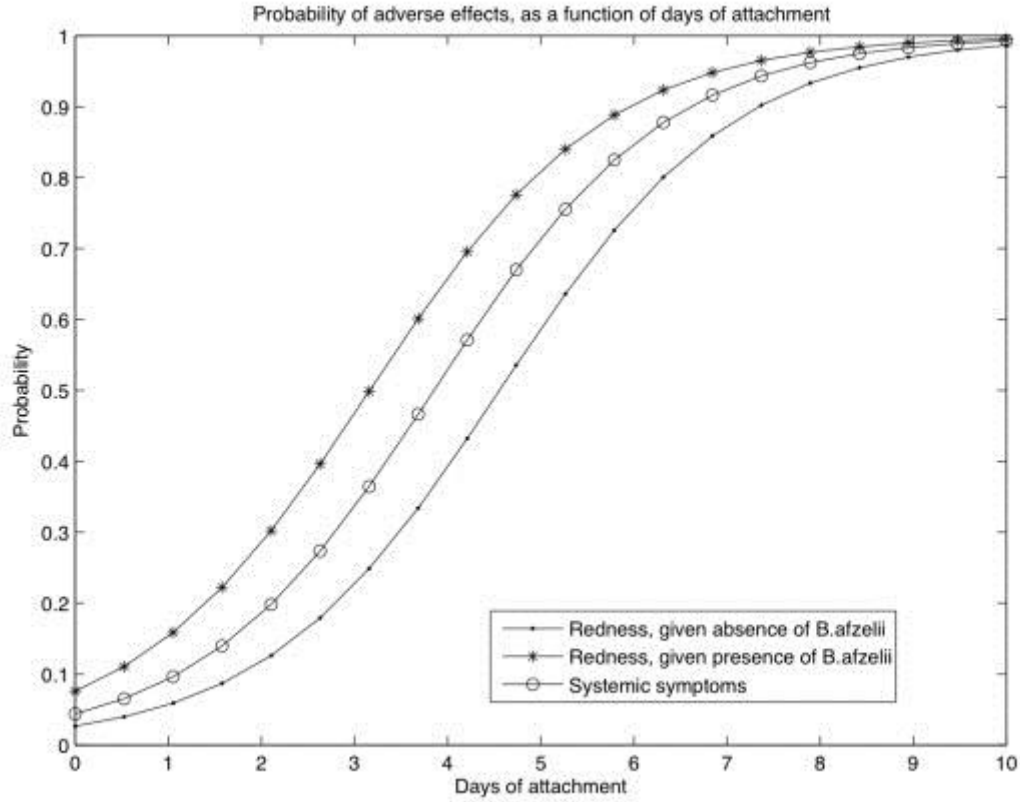
Relative risks were calculated by dividing incidence rates of exposed by incidence rates of unexposed participants. Confidence intervals and p-values were calculated using Fisher's exact test. P-values below 0.05 (*) were regarded as significant.

Figure 1. Prevalence of microorganisms in different tick stages.



Ticks of different life stages were collected from humans and microorganisms were detected and identified using PCR followed by RLB. Bars indicate 95% confidence intervals calculated with Fisher's exact test.

Figure 2. Probability of adverse effects after a tick bite



Described as a function of days of attachment and accounting for the presence/absence of *B. afzelii*. The formula describing this relationship can be found in the results section

Part II

Innovation: Teleradiology

Chapter 5

Fracture diagnostics, unnecessary travel and treatment:
A comparative study before and after the introduction of teleradiology in a remote general practice

Jac. J.W.M. Jacobs, Jan P.A.M. Jacobs, Eric van Sonderen, Thys van der Molen and Robbert Sanderman
*BMC Fam Pract. 2015 May 6;**16**(1):53. doi: 10.1186/s12875-015-0268-z.*

Abstract

Background. Teleradiology entails attainment of x-rays in one location, transfer over some distance and assessment at another location for diagnosis or consultation. This study documents fracture diagnostics, unnecessary trips to the hospital, treatment and number of x-rays for the years 2006 and 2009, before and after the introduction of teleradiology in a general practice on the island of Ameland in the north of the Netherlands.

Methods. In a retrospective, descriptive, observational before and after study of the introduction of x-ray facilities in an island-based general practice, we compared the number of accurately diagnosed fractures, unnecessary trips, treatments and number of x-rays taken in 2006 when only a hospital x-ray facility was available 5 hours away with those in 2009 after an x-ray facility became available at a local general practice. All patients visiting a general practice on the island of Ameland in 2006 and 2009 with trauma and clinical suspicion of a fracture, dislocation or sprain were included in the study. The initial clinical diagnoses, including those based on the outcomes of x-rays, were compared for the two years and also whether the patients were treated at home or in hospital.

Results. A total of 316 and 490 patients with trauma visited a general practice in 2006 and 2009, respectively. Of these patients, 66 and 116 were found to have fractures or dislocations in the two years, respectively. In 2006, 83 x-rays were ordered; in 2009, this was 284. In 2006, 9 fractures were missed; in 2009, this was only 2. In 2006, 15 patients with fractures or dislocations were treated at the general practice; in 2009, this had increased to 77.

Conclusion. Since the introduction of teleradiology the number of missed fractures in patients visiting the general practice with trauma and the number of the unnecessary trips to a hospital are reduced. In addition more patients with fractures and dislocations can be treated in the general practice as opposed to the hospital.

Background

Teleradiology is the electronic transmission of radiological images from one location to another for the purpose of interpretation and/or consultation. This technique has proliferated in many countries but not yet in the Netherlands[1]. In the Netherlands, all x-rays are obtained in hospitals or diagnostic centres and subsequently assessed by radiologists. In many other countries, x-rays are obtained in the general practices themselves and reviewed by the general practitioners (GPs). When judged necessary, a radiologist may sometimes be consulted with the use of teleradiology [2,3].

In the Netherlands, an average of 42-43 per 1000 patients experience new traumas and visit a general practice annually: 27 with strains on average; 13-14 with fractures on average; and 2 with dislocations on average [4]. For trauma patients with suspected fractures or dislocations, Dutch healthcare guidelines require x-ray confirmation of the fracture or dislocation in hospital, followed by either conservative or surgical treatment by a surgeon[5,6]. The GP in the Netherlands today normally refers the patient to the hospital for x-ray. Trauma patients with suspected strains, in contrast, are typically treated only on the basis of clinical signs by general practitioner.

In a relatively remote location, the island of Ameland in the north of the small country of the Netherlands, teleradiology was recently introduced. Prior to 2007, all patients with suspected fractures received plaster splints at the general practice for immobilization or when necessary following deformity correction, and were sent to the hospital for further x-ray examination (which is in keeping with the normal procedure in The Netherlands). These patients frequently returned with the same plaster splints following x-ray confirmation of the fracture or successful repositioning. In fact, at that time, such trauma patients often only travelled to the hospital to have the x-rays taken. Given that the hospital takes a ferry trip to be reached, the threshold for a referral to the hospital was (and is) very high. The physical examination at the general practice had to strongly suggest a fracture or dislocation for referral to the hospital; fractures of the phalanx (i.e., fingers or toes) or habitual shoulder dislocation were often treated in the general practice without x-ray back then.

Medical diagnosis always has the risk of missing something, on the one hand, versus unnecessary referral, on the other hand (i.e., patients travelling to hospital for nothing in the end). This dilemma and particularly the high threshold for ordering supplemental diagnostics in a rural location as Ameland was expected to disappear when a GP obtained access to an x-ray facility and introduced teleradiology to communicate with a hospital (i.e., radiologists and surgeons).

Telemedicine has received considerable attention in the research literature but teleradiology much less [3]. In the present study, it was therefore decided to investigate the following question: what is the influence of the introduction of an x-ray facility in a remote GP practice on accurately diagnosed fractures, hospital visits, number of x-rays and treatment. It was expected that the number of missed fractures and unnecessary hospital referrals (trips to the hospital) would decline with the introduction of teleradiology. We did not expect huge changes in treatment and number of x-rays, i.e. that clinical indications for x-rays would be unaffected.

Methods

Setting and preparation

Ameland is an island with 3500 inhabitants and 20 times as many tourists during the busy season (summer). Medical care is delivered at two general practices, which also in cases of emergencies serve the function of emergency room. The nearest hospital is in Dokkum on the mainland, with a travelling time of approximately five hours, including a ferry trip.

The teleradiology facility is installed in one of the two general practices but available for use with all patients — including those from the other GP on the island and tourists. When needed, the x-rays are taken by a trained radiographer working in the general practice and digitally transmitted to the hospital in Dokkum where the x-ray information is evaluated and interpreted by a trained radiologist. The radiologists are available during regular office hours and for emergency situations 24 hours a day, 7 days a week. In consultation with the surgeon in the hospital, it is decided whether the patient in question can be treated in the general practice under the supervision of a surgeon or should be treated in hospital. The radiographer is a full-time employee of the general practice and responsible only for the taking of x-rays and not for the interpretation of these.

The radiologist always responds digitally on the same day and, if necessary, directly by phone. The radiologist may sometimes give the radiographer special instructions for the x-rays by phone. The hospital's x-ray protocol is followed. The radiographer receives ongoing feedback on the quality of the x-rays taken. And the radiographer receives annual training at the hospital.

The indications for an x-ray are twofold, namely: 1) trauma in the form of fractures or dislocations and 2) non-trauma requiring x-ray for monitoring or surgical purposes (e.g., x-ray in cases of hip degeneration, knee problems, and lung carcinoma).

In the present setting, the GP was trained as a radiation expert. Together with the Institute of Nuclear Services for Energy, Environment and Health in the Netherlands, the GP is also responsible for all radiation hygiene and safety within the general practice. The costs of the x-rays and the honorarium for the radiologist are covered by the patient's insurance. The x-rays made in the general practice are stored together with any x-rays made at the hospital in the Picture Archiving and Communication System (PACS) of the hospital.

Study design

In a retrospective, descriptive, observational before and after study, we compared the health outcomes for patients who visited the general practice with a recent trauma in 2006 — the year before the introduction of the teleradiology facility — and patients who visited the GP with a recent trauma in 2009 — the second year after the introduction of the facility and the most recent year for which data was available. Only traumas related to the musculoskeletal system (i.e., strains, fractures and dislocations) were investigated.

Study population, data collection and material

Retrospective, all the patients who visited the GP in 2006 and 2009 with the above mentioned traumas were selected from the Promedico database by the GP himself. On the basis of their initial clinical signs, the patients were categorized into six groups: (1) clear deformity, (2) pain due to weight bearing or axial compression, (3) local pressure pain, (4) haematoma, (5) stiffness, (6a) no disorder or (6b) immobilized. Patients in group 1 definitely had a fracture or dislocation and needed treatment as soon as possible — preferably following x-ray confirmation of the condition. Patients in group 2 had suspected fractures which had not yet been confirmed but called for an x-ray. Patients in group 3 had strains but also the possibility of fracture(s) and were instructed to return for re-examination if still in doubt about the diagnosis after two days [4,5]. Patients in groups 4, 5 and 6a showed minimal trauma and no apparent fracture. The patients in group 6b had been immobilized (re-trauma), which precluded physical examination in the general practice.

Information was also gathered from the above mentioned database on the clinical diagnosis, whether an x-ray was obtained or not, undertaken treatment, location of treatment (hospital or general practice), the practice with which the patient was registered and the x-ray was ordered (GPs from both general practices on the island could order x-rays) and final diagnosis. A physician assistant contacted those patients for whom no final information on the medical outcome was available to obtain this information by telephone (i.e., both tourists and islanders who did not return to the

practice following consultation for the relevant trauma were contacted to obtain required follow-up information).

Subsequently the GP anonymized the selected data (including the information gathered by the physician assistant) and a medical student imported these data into a registration system of the University Medical Centre Groningen. *International Classification of Primary Care* (ICPC) codes were assigned. The initial ICPC diagnoses (diagnosis at the moment of treatment) were then compared to the final ICPC diagnoses (diagnosis collected after a period by the physician assistants phone call or from the medical outcome).

Ethics statement

Because the study is retrospective with data anonymized from patients records, it falls outside the Medical Research Involving Human Subjects Act (WMO) in the Netherlands and does not need to be approved by a medical ethics committee. We followed the Health Research Guidelines (Gedragscode Gezondheids Onderzoek 2004), which are based on the Medical Treatment Law (WGBO) and the Privacy Protection Law (Wbp). The use of anonymized data in medical research that cannot be traced back to individual patients is allowed. This study is based on anonymized medical records of the GP, which were completed by information obtained from patients after informed consent by a physician assistant.

Results

In 2006 and 2009, respectively, 316 and 490 patients visited the general practice with recent traumas. From these 56 (2006) and 77 (2009) were contacted by phone; 4, 7 respectively could not be reached and one patient in 2009 refused to answer the questionnaire. Hence, our sample consists of 312 patients in 2006 and 482 patients in 2009.

In 2006, 83 patients (26.6%) were referred to hospital. For 41 of them (49.4%), this trip proved unnecessary; they did not have fractures and were treated further by the GP. In 2009, 39 patients (8.1%) were referred to hospital: 3 of these directly without x-ray in the general practice; 2 with a CT scan indication due to high-energy trauma; and 1 with a complicated tibia/fibula fracture. In retrospect, the two trips for the patients with the CT indications (0.4%) proved only precautionary. In 2006, a total of 83 x-rays were taken on 26.6% of the total number of patients visiting the general

practice for recent trauma. In 2009, 281 x-rays were taken on 57% of the total number of trauma patients visiting the general practice.

In 2006, 66 (21%) of the patients had fractures or dislocations and 9 (13.6%) of these were missed. In 2009, 116 (24.1%) of the patients had fractures or dislocations and 2 (1.7%) of these were missed. The general practitioner treated 15 patients (22.8%) without x-ray confirmation in hospital in 2006 and 77 patients (66.4%) after x-ray confirmation in the general practice itself in 2009.

Table 1: Trauma patients visiting the general practice in 2006 and 2009

	2006	**2009**
Number of trauma patients	**312**	**482**
X-rays	**83 (26.6%)**	**281 (58.3%)**
Hospital referrals	**83 (26.6%)**	**39 (8.1%)**
Unnecessary trips to the hospital	**41 (13.5%)**	**2 (0.4%)**
Fractures or dislocations	**66 (21.2%)**	**116 (24.1%)**
Fracture or dislocation treatment by the GP	**15 (22.7%)[1]**	**77 (66.4%)[1]**
Missed fractures	**9 (13.6%)[1]**	**2 (1.9%)[1]**

[1] Percentages of fractures

The majority of the fractures were radius/ulna, phalanx, metacarpal and tibia/fibula fractures (see Table 2). The 9 missed fractures in 2006 consisted of 3 radius/ulna, 4 tibia/fibula and 2 vertebral fractures. These fractures were much more severe than the 2 missed toe phalanx fractures in 2009.

Table 2: Fractures and/or dislocations in 2006 and 2009

Year	2006			2009		
	Total (%)	Referred (%)	Missed (%)	Total (%)	Referred (%)	Missed (%)
Total fractures	66	42 (63.6%)	9 (13.6%)	116	37 (31.9%)	2 (1.7%)
Radius/ulna	13 (21.7%)	10 (76.9 %)	3 (23.1%)	39 (36.1%)	14 (35.9%)	0
Tibia/fibula	10 (15.2 %)	6 (60.0 %)	4 (40.0 %)	12 (11.1%)	3 (27.3 %)	0
Metacarpal /phalanx	26 (43.3%)	13 (50.0 %)	0	24 (22.2%)	5 (23.8 %)	2 (8.3%)
Others	17 (25.8%)	12 (70.6%)	2 (11.8 %)	33 (30.6%)	15 (35.7%)	0

The breakdown of the trauma patients with suspected fracture or dislocation on the basis of initial physical examination is as follows (see Table 3). In 2006, 23 trauma patients (8.5%) were identified as having deformities (group 1); in 2009, this was 37 (9.6%). In 2006, 20 of these patients were sent to the hospital for x-ray confirmation of the deformity after correction and immobilisation at the general practice; 3 of them had habitual shoulder dislocations and were treated by the GP without a visit to hospital. In 2009, 36 of the 37 trauma patients with suspected deformities (group 1) had an x-ray confirmation at the general practice before correction and/or immobilisation of the dislocation and x-ray checking again afterwards. In the end, 31 of the these patients — including the patient mentioned above with the complicated tibia/fibula fracture — were sent to hospital for further treatment in 2009 and 6 were treated solely in the general practice.

Table 3: Physical examination, diagnosis and treatment of trauma patients in 2006 and 2009

	2006						2009					
Physical examination	**1: Defor-mity**	**2: Axial compression pain**		**3: Local pressure pain**		**Total: 1, 2, 3 2006**	**1: Defor-mity**	**2: Axial compression pain**		**3: Local pressure pain**		**Total: 1, 2, 3 2009**
Number of patients	23	67		181		271	37	162		186		385
Suspicion of fracture[1]		**Direct**	**After two days**	**Direct**	**After two days**			**Direct**	**After two days**	**Direct**	**After two days**	
No	0	9	0 +4[2]	181	165 +5[2]	165 +9[2]	0	0	0	168	119 + 2[2]	119 + 2[2]
Yes	23	58	5	0	11	97	37[3]	162	0	16 +2[4]	47	264
Treatment by GP without x-ray	0	0	4	181	170	174	0	0	0	168	121	121
No fracture												
Fracture	3[5]	12[6]	0	0	0	15[5,6]	0	0	0	0	0	0
Result of x-ray (hospital in 2006 and general practice in 2009):	0	31	2	0	8	41	0	103	0	6 + 2[4]	47	158
No fracture												
Fracture	20	15	3	0	3	41	36 + 1[3]	59	0	10	0	106
Treatment by GP after x-ray:	0	31	2	0	8	41	0	103	0	6 + 2[4]	47	158
No fracture												
Fracture	0	0	0	0	0	0	6	53	0	10	0	69
Treatment Hospital: fractures (only)	20	15	3	0	3	41	31	6	0	0	0	37

[1]Fractures = Fractures and/or dislocations
[2]Missed fractures
[3]One patient with a complicated tibia/fibular fracture was sent directly to the hospital without obtaining an x-ray at the general practice.
[4]Two patients with a high-energy trauma were sent directly to the hospital (CT-scans indicated).
[5]Three patients with habitual shoulder dislocation were treated by the GP without x-rays.
[6] Twelve patients with phalanx fractures were treated by the GP without x-rays.

The group of patients with axial compression pain (group 2) consisted of 67 (24.7%) patients in 2006 and 162 (42.1%) in 2009. Of these patients, 46 and all 162 had x-rays taken for 15 and 59 fractures, respectively. In 2006, 5 patients returned after two days for repeated x-ray and three of them were found to have fractures.

The group of patients with local pressure pain (group 3) consisted of 181 (66.8%) patients in 2006 and 186 (48.3%) in 2009. Of these patients, 16 of 2009 had an x–ray taken directly with 10 fractures and 11 and 47, respectively, had x-rays taken after two days. In 2006, 3 of these 11 patients were found to have fractures; in 2009, none of the 47 patients undergoing follow-up x-ray were found to have fractures. In 2009, 19 patients with a new trauma which occurred while in plaster immobilisation for a previous fracture (group 6b) had an immediate x-ray; 8 of them had a re-fracture and were further treated at the general practice. The group of patients with minor trauma (group 4, 5, 6a) consisted of 41 patients in 2006 and 97 in 2009. In 2006 one patient complained of stiffness and was immobilized transported to the general practice by an ambulance because of a high energy trauma. He was sent directly to the hospital with a cervical vertebra fracture suspicion where it was confirmed and treated.

Figures 1 and 2 in the Appendix connect the results presented in Tables 1 and 3. Clear differences in the thresholds for x-ray (82 at hospital in 2006; 281 at GP in 2009) can be seen. Doubt about a fracture (followed by a re-examination after two days) existed for all of group 3 and part of group 2 in 2006, but only for part of group 3 in 2009. Similarly, clear differences in the treatment of fractures by the GP under the supervision of a surgeon can be seen zero in 2006; 69 in 2009. Moreover, all of the fractures for group 3 and most of those for group 2 could be treated by the GP under the guidance of a surgeon in 2009 (highlighted in red).

Discussion

Summary

There is a clear difference in outcomes between 2006 and 2009. Fewer fractures were missed and no severe fractures whatsoever were missed. Fewer patients had to make the unnecessary trip to the hospital five hours away. In 2006, 41 patients (13.1%) were found at the hospital to not have a fracture. In 2009, only 2 patients (0.4%) with a CT-scan indication were found to not have a fracture and therefore had travelled unnecessarily to the hospital. These differences ran parallel with the introduction of teleradiology into the general practice and yielded significant benefits for patients.

A further benefit of this introduction was that more fractures and dislocations could be treated by the GP. In 2009, 77 of the patients with fractures or dislocations (66.4%) could be treated by the GP under the supervision of a surgeon. In 2006, no patients could be treated in this manner. Moreover, in 2006 15 patients (22.5%) with mostly phalanx fractures or dislocations were treated by the general practitioner without x-ray confirmation of the fractures or dislocation, which is not in accordance with Dutch guidelines which require an x-ray confirmation[5,6].

An unexpected advantage of teleradiology was that immobilised patients with re-fractures as a result of new traumas could be diagnosed and treated by the GP. In previous years, this would have required a trip to the hospital.

An unexpected side effect was that more x-rays were taken with the availability of teleradiology, particularly for patients with uncertain clinical signs of fracture (patients in groups 2 and 3). Following the introduction of teleradiology, the percentage of patients with an unclear fracture returned for re-examination became more than twice as much than before. This suggests that the introduction of teleradiology created demand. However the introduction of teleradiology enables general practitioners to work in keeping with Dutch guidelines[5,6] and saves patients time, money and the anxiety of not knowing the outcome of a traumatic event.

The number of patients that visited the general practice with recent trauma is higher in 2009 compared to 2006. This increase can be partly explained by different weather conditions in 2009 which probably caused more risky outdoor activities as evidenced by the number of more severe (radius-ulna) fractures in 2009. In addition we cannot rule out that patients who previously went directly to the hospital prefer to visit the general practice after the introduction of teleradiology.

Study strengths and limitations

Our study is the first to examine accurately diagnosed fractures, unnecessary trips to the hospital, treatment and number of x-rays before and after the introduction of teleradiology in a general practice. Information was obtained on initial and final diagnosis, subsequent treatment and number of x-rays made. The detailed description of the clinical signs and outcomes for trauma patients consulting a general practice before and after the introduction of teleradiology is thus a major strength of the present study. An additional strength is that the observed changes in the outcomes did not arise from differences in the x-ray examination procedures because, as usual in the Netherlands, all x-rays were interpreted by trained radiologists — both before and after the introduction of teleradiology.

A limitation is that we did not carry out a (randomized) controlled experiment, because of medical ethical reasons. Hence the difference in outcomes can in theory not only be attribute to the introduction of teleradiology. However since the GP's, radiologists, surgeons, physical assistants and procedures were the same in 2006 and 2009, we have strong reasons to believe that the documented changes in outcomes are due to the introduction of teleradiology in the general practice.

Another possible limitation is that the samples from 2006 and 2009 were obviously obtained from different populations. Given that we could not contact all of the patients for follow up, there may have been more missed fractures. The number of research years (i.e., 2006 versus 2009) is small and also a possible limitation on the present study. Due to changes in the staffs of the general practice and the radiologists of the hospital radiology department in January 2010, it was not possible to continue data collection beyond 2009.

Comparison to existing literature

Research on the introduction of teleradiology into primary healthcare is scarce and typically confined to the implementation of teleradiology and its costs, organization, logistics, management and disadvantages [1,3,7,8,9,10,11]. Benefits have also been described but are mainly based on the opinion of doctors and patients [9,12]. To the best of our knowledge, fracture diagnostics, unnecessary trips to a hospital and subsequent treatment before and after the introduction of an x-ray facility in combination with teleradiology into a general practice has not been detailed studied in patients with acute trauma [13]. Studies of other telemedicine applications exist, including studies of the effects of telecardiology, videoconferencing and teledermatology [7,11,12,14,]. The results of these studies are not sufficient, however, to justify the more widespread introduction of teleradiology into primary healthcare[7,11].

Implications for future research and clinical practice

In a companion study, we performed a cost-benefit analysis of teleradiology and found its introduction into a general practice to result in a considerable reduction of costs not only for patients (111,000 euros per year) but also for health insurance companies (at least 89,000 euros per year)[15].

Future research should aim to implement teleradiology into more general practices and investigate whether the current procedure of having a trained radiologist interpret the x-rays can be expanded to allow GPs to be trained to also interpret x-rays. In addition, future research should certainly investigate the quality of the

treatment by a GP, using teleradiology under the supervision of a surgeon, relative to the quality of the treatment by a surgeon in hospital.

Conclusion

The present paper study suggests that teleradiology in a general practice has clear benefits in terms of reducing the number of missed fractures, unnecessary trips to the hospital and increasing the possibilities for treatment at home. Teleradiology is thus a good example of healthcare which can be transferred from hospitals to primary healthcare centres, despite the finding that, following the Dutch Guidelines more x-rays were requested — particularly for patients with uncertain clinical signs of fractures. This conclusion presumably holds for other general practices in rural areas and other countries as well.

Acknowledgements

We thank Frank Baarveld for making the registration system available; Felix Poppelaars for entering the data into the registration system; and Marian Iemhoff-Bakker for interviewing the patients.

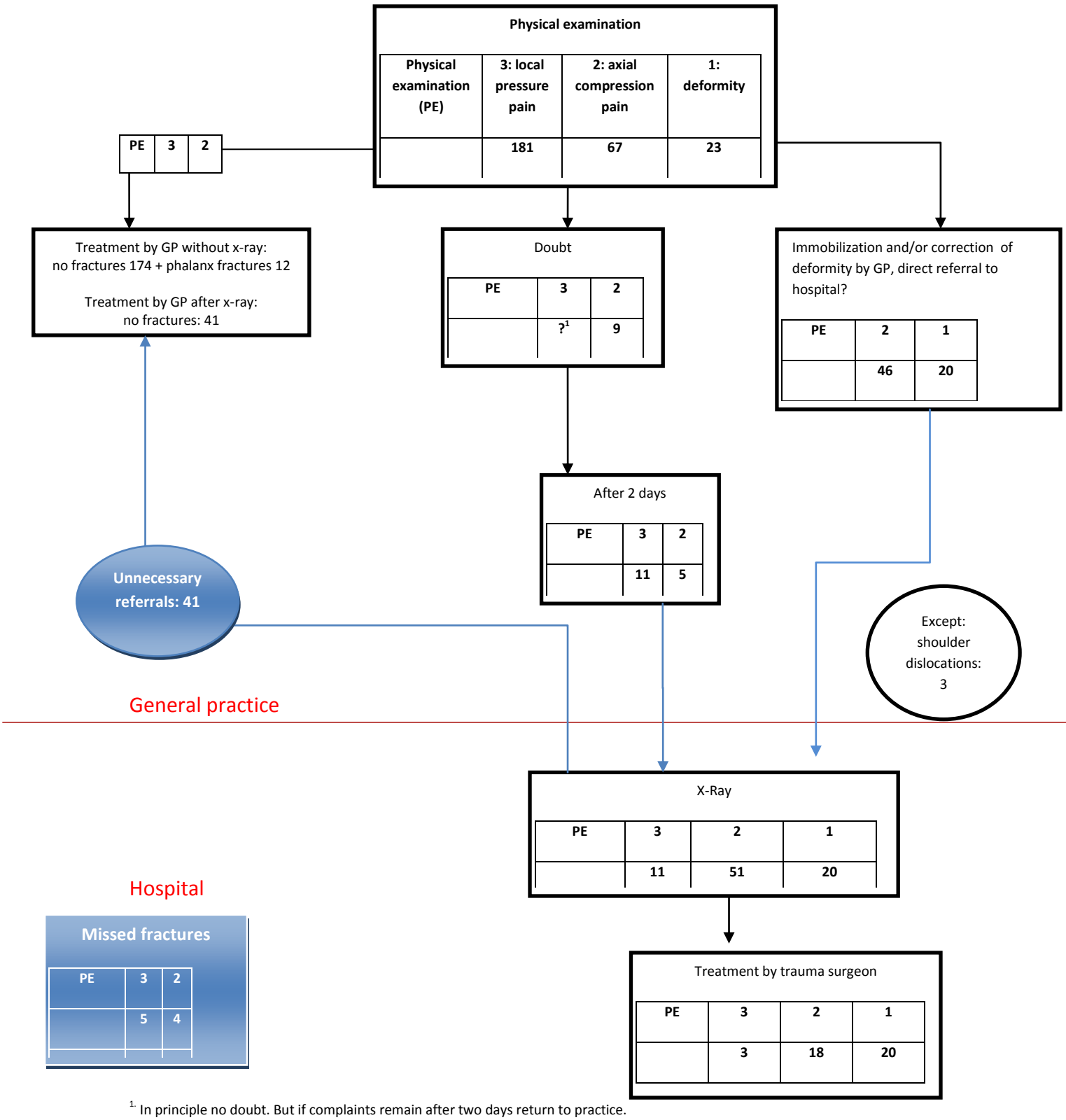
References

1. Mun SK, Tohne WG, Platenberg RC, Choi I. **Teleradiology and emerging business models.** *J Telemed Telecare* 2005; **11(6)**: 271-5.
2. Knop FK, Staunting JA. **The benefits of diagnostic imaging in general practice.** *Ugeskr Laeger* 2006; **2**: 794-8.
3. Ekeland AG, Bowes A, Flottorp S. **Effectiveness of telemedicine: a systematic review of reviews.** *Int J Med Inform* 2010; **79**: 736-71.
4. Lisdonk vd EH, Bosch vd WJHM, Lagro-Janssen ALM, Schers HJ. **Ziekten in de Huisartsenpraktijk [Illnesses in General Practice].** Reed Business , fifth revised version 2008. (Dutch)
5. Belo J, Buis P, Rijn van R, Sentrop-Snijders E, Steenhuisen S, Wilkens C, Geijer R, Loogman M. **NHG-standaard Enkelbandletsels [NHG-guidelines Ankle Injuries].** *Huisarts Wet* 2012; **55(8)**: 352-356. (Dutch)
6. Keeman JN, Schadé E. **Spoedeisende Geneeskunde voor de Huisarts [Emergency Medicine for the GP].** Bohn Stafleu Van Loghum, second revised version 1997. (Dutch)
7. Norum J, Pedersen S, Størmer J, Rumpsfeld M, Storma A, Jamissen N, et al. **Priorisation of telemedicine services for large scale implementation in Norway.** *J Telemed Telecare* 2007; **13**: 185-92.
8. Char A, Kalyanpur A, Puttanna Gowda VN, Bharathi A, Singh J. **Teleradiology in an inaccessible area of northern India.** *J. Telemed Telecare 2010***; 16(3)**:110-3
9. Johansen I, Breivik E **[English translation of title: Is teleradiology service in primary health care cost-effective?].** *Tisskr Nor Laegebforen* 2004; **124 (19)**:2490-2
10. Krestin GP, Pieterman H. **Teleradiologie: bedreigingen en kansen [Teleradiology: threats and opportunities]**. *Ned Tijdschr Geneeskd* 2011; **155**: A2997. (Dutch)
11. Hailey D, Roine R, Ohinmaa A. **Systematic review of evidence for the benefits of telemedicine.** *J Telemed Telecare* 2002; **8**(suppl 1): S1:1-7.
12. Moffat JJ, Eley DS. **The reported benefits of telehealth for rural Australians** . *Aust Health Rev* 2010; **34(3);** 276-81.
13. Heijden van der JP, Keizer de NF, Bos JD, Spuls PI, Witkamp L. **Teledermatology applied following patient selection by general practitioner in daily practice improves efficiency and quality of care at lower costs.** *Br J Dermatol* 2011; **165**: 1058-65.
14. McGill AF, North JB. **Teleconference fracture clinics: a trial for rural hospitals.** *ANZ J Surg* 2012; **82**: 2-7.

15. Jacobs JJWM, Jacobs JPAM, Wiersma D, Sanderman R. **Teleradiologie in de huisartenspraktijk op Ameland. Een kosten-baten analyse [Teleradiology in general practice at Ameland. A cost-benefit analysis].** *Ned Tijdschr Geneeskd* 2013; **156** (51): A5428. (Dutch)

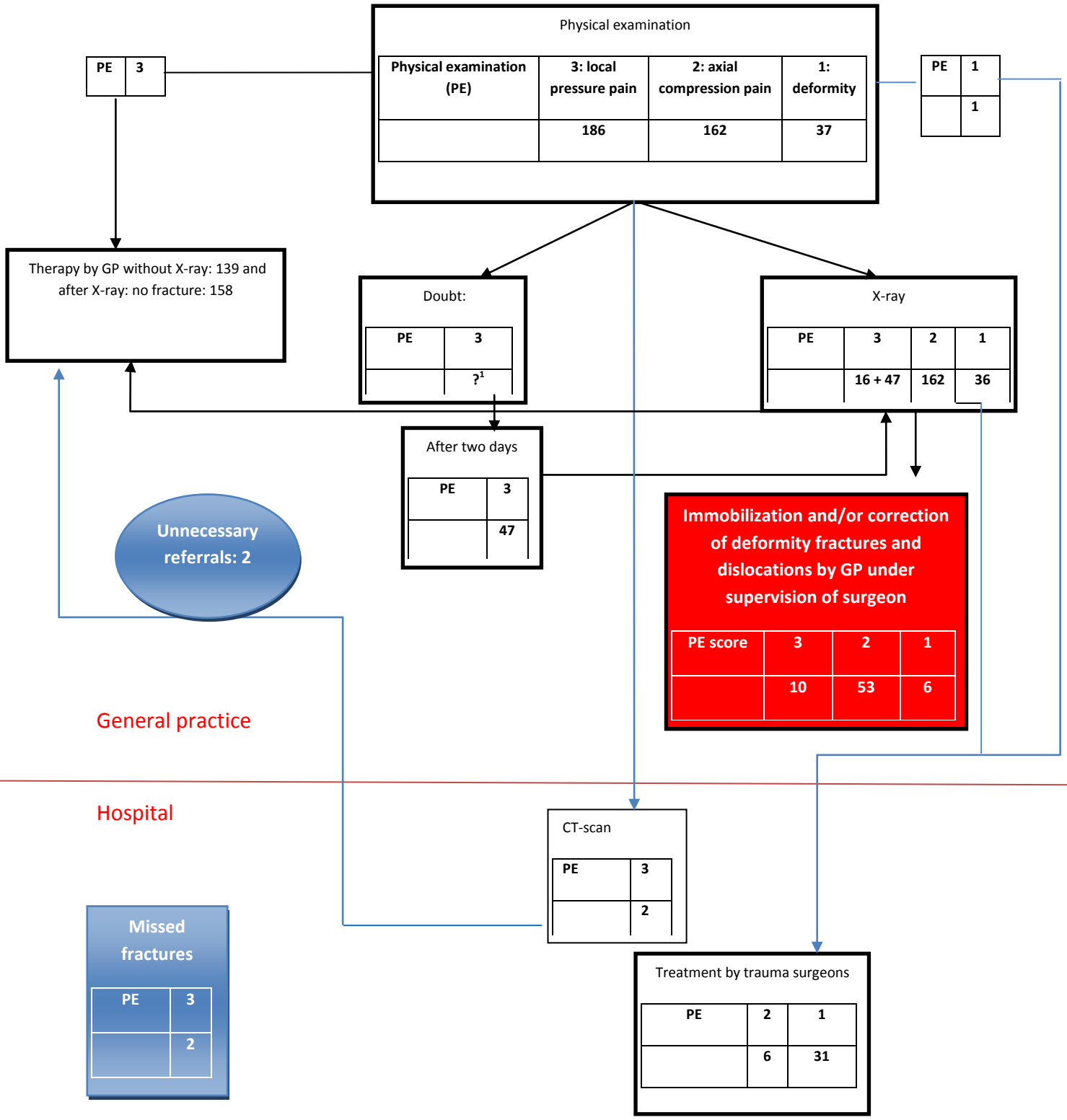
APPENDIX

Figure 1. Flow chart for 2006



1. In principle no doubt. But if complaints remain after two days return to practice.

Figure 2. Flow chart for 2009



1. In principle no doubt. But if complaints remain after two days return to practice.

Chapter 6

Teleradiology in the general practice at Ameland:

A cost-benefit analysis

Published in Dutch with original title:

Teleradiologie in de huisartsenpraktijk op Ameland: Een kosten baten analyse.

Jac. J.W.M. Jacobs, Jan P.A.M. Jacobs, Doede Wiersma and Robbert Sanderman

Ned Tijdschr Geneeskd 2013;156(51):A5428.

Abstract

Objective: To calculate the costs and benefits of the introduction of teleradiology at a general practitioner's office on the Dutch island of Ameland from the perspectives of three different entities: (a) a family doctor (investor); (b) patients; (c) health insurance companies.

Design: Descriptive, cost-benefit analysis.

Methods: For the year 2009, one and a half years after the introduction of a teleradiology facility at a family practice on Ameland, the operational and financing costs, the patients' saved travel time and expenses and the teleradiology costs for health insurance companies were compared to the assumed costs without teleradiology.

Results: In 2009, 426 x-rays were taken at the family practice, of which 242 were trauma's and 185 concerned non-trauma cases. With a €100 reimbursement per x-ray taken during office hours (€200 during evening- and weekend hours) the benefits for the family doctor (investor) were €46,698 and the costs amounted to €45,710, a positive balance of €980. Patients' saved travel time and expanses translated into and amount of €111,068. Health insurance companies save a minimum of €89,265 on diagnosis and treatment reimbursements.

Conclusion: The introduction of teleradiology at a family practice on Ameland resulted in considerable costs reductions for both patients and health insurance companies. This method of diagnosing can be expanded in the future, especially to remote areas where hospitals are at great distances. Also part of the diagnosing and treatment could be conducted at reduced costs for primary healthcare.

Introduction

Secondary diagnosis patients no longer need to travel to hospitals due to advanced technological developments in recent years in the ICT area. General practitioner and specialist can exchange data digitally and determine on a treatment this way. This form of peer communication is an essential part of Dutch healthcare and has already been implemented in, amongst other areas, cardiology and dermatology[1].

Taking x-rays in general practices is well established in many western European countries[2]. Also, teleradiology, the system where x-rays are taken in one place and reviewed for diagnosis and consultation in another[3], is not an unknown phenomenon in the medical world[4].

On Ameland all medical care is provided by 2 general practitioner's offices that due to long travel times to the nearest hospital, both fulfill the role of an Emergency Room. In 2007 one of the general practices set up a teleradiology pilot study following the extra care deriving from this ER role. The project was centralized around three research questions: (a) is teleradiology possible within primary healthcare without losing medical-technical quality of the given care?; (b) does teleradiology lead to satisfying results for patients?; (c) does teleradiology produce cost savings? This article addresses this last question and shows a cost-benefit analysis of teleradiology in a family practice.

Methods

Design

Since 2007 it is possible to take x-rays in one of the general practices on Ameland and send them to the radiology department of the *De Sionberg* Hospital in Dokkum via glass fibre cables. All general practitioners on the island can request x-rays. These images are reviewed by a radiologist, who communicates his results back to the requesting general practitioner. In case another specialist needs to be consulted by the general practitioner, this will be done immediately after the results from the x-rays are known.

The cost-benefit analysis of teleradiology was performed over the year 2009, 1,5 years after the introduction of this new facility. This was also the first year we had access to the complete data. Information about the time period before the introduction is unknown and recent data from 2010 and 2011 have not been processed so far.

We divided the patients who had x-rays done in 2 groups. The first group consisted of trauma patients with clinical suspicion of fractures or luxation (dislocation or axial pain, loss of function, swelling or pressure pain). Without teleradiology these patients would have had been sent to the ER of a hospital to be seen by a traumatologist (for the ankle diagnosis the *NHG*-standard –Dutch College of General Practitioners- was used). The second group consisted of patients visiting on request of a specialist for check-up x-rays or for extra diagnosis due to persistent coughing or degeneration of the joints. Without teleradiology the x-rays of these patients would have only been seen by a radiologist in the hospital. Exceptions to this are the images of the check-up x-rays and the x-rays taken by the general practitioner as a basis of a referral to a specialist.

This article draws up a cost-benefit analysis, in which both costs and benefits are expressed in money. In the computation we followed the recommendations from an earlier article on teleradiology to calculate the costs and benefits separately for the involved entities[5]. In our research these are: the family doctor (investor); the patients and the health insurance companies.

General practitioner

The general practitioner was the investor (financer) in the teleradiology facility in this research. The costs that were made consisted of financing costs for the purchase, an extra loan and depreciations. There were also operational costs, consisting of maintenance of the equipment, costs for extra personnel, costs for the use of the glass fibre cable and technical quality control costs. The benefits consisted of reimbursements for x-ray examinations per patient, paid by the health insurance companies (€100 per x-ray taken during office hours and €200 during evening- and weekend hours) and a reimbursement for any extra consults (€9 per consult).

Patients

Thanks to a teleradiology facility on the island patients save travel time and expenses, since they do not need to travel to a hospital on the main land anymore to have their x-rays taken. The estimated cost savings were determined by the “Travel cost method”[6,7]. We apply the next assumptions as a starting point:

- Patients went to the hospital closest to the island to have their x-rays taken, this is the Dokkum hospital.
- Patients traveled by car to an average cost of €0,40 per km.

- Patients were accompanied by 1 adult, because they were not capable of travelling independently (for example, due to a fracture or bad physical conditions).
- Patients spent 8h on travel and hospital time.
- Patients' time is valuable. In economic terms the worth is valued based on its most likely alternative. For the active employed population (15-65 yrs) this is work. For this age group we valued the saved travel time and hospital time according to the average wage level per hour in the Netherlands in 2009 that amounted to €29,79 according to Eurostat. Since it concerns the value of the employees, in other words their revenues minus the deduction of taxes and social security premiums, a net income of €15 an hour was applied as valuation reference. Pensioners and students value their time differently. Alternative leisure activities for pensioners can be part-time continuations of their employment after 65, executing consulting work or volunteering. Since there was no data on these alternatives available, we valued the time of pensioners at an average of half of the net income of the employed patients. The best alternative activity for students is studying. The time value of students was estimated at €2,50 an hour.
- The travel costs for islanders was adjusted according to the reduction they receive on the ferryboat fares.
- The ferryboat fares are higher during (tourist) high season than they are in low season. A 50/50-devision of the amount of tourists vs. islanders was assumed.

The special location of Ameland, a Dutch *Wadden* island, implies that travel time and costs for visiting a hospital are higher than for other remote areas. Therefore in comparison also the costs for an equal size general practice on the main land without tourists were determined.

Health insurance companies

In order to determine the savings for the health insurance companies the costs for x-ray examinations and treatment after the introduction of teleradiology were compared to the costs that would have been made without the use of teleradiology. The health insurance companies paid the general practitioner the service cost for taking the x-ray, the radiologist the consult cost for assessing the x-ray, and in case of referral to a specialist an extra cost, the *diagnose behandeling combinatie (dbc)* – diagnosis treatment combination – excluding the radiology component in the *dbc* to

avoid double-counting. In case patients were referred to the specialist, the reimbursement for the radiologist was included in the *dbc* of the specialist. Without the use of teleradiology the costs consisted of the radiologist's fee plus the hospital costs for taking the x-ray or, if applicable, the *dbc* of the specialist.

An independent researcher (F.P.) recorded in retrospect the 'International Classification of Primary Care' (ICPC)-code for all patients that had an x-ray taken in 2009, in a registration system developed by the general practitioner's faculty of the *UMCG* (University Medical Center Groningen). This code was used to determine the indication for the x-ray. The code was used for trauma patients to retrieve the *dbc's* of *De Sionberg* hospital in Dokkum. This was done in cooperation with the *dbc*-expert of that hospital. Comparisons to the tariffs of the *Nederlandse Zorgautoriteit* (the Dutch Healthcare Authority) showed that specialists chose the cheapest *dbc*-alternative, the 'conservative treatment'. This includes treatments that can be done by primary healthcare providers.

Results

In 2009, 426 x-rays were taken in the general practice. It concerned 287 islanders and 139 non-islanders; 241 x-rays were trauma related and 185 were non-trauma related. The total is comparable to 420, 407 and 393 examinations done in respectively 2008, 2010 and 2011. In 2009, 98 patients (40%) suffered a fracture or luxation, of which 23 were referred to a surgeon, be it either directly for surgery or for a 1 week check-up after repositioning. The remaining 75 patients were treated by the general practitioner, under supervision of a specialist. 7 X-rays were requested by a specialist and 5 patients without trauma were referred to a specialist based on the taken x-ray.

Before 2007 a patient with a wrist fracture with dislocation was fitted for a cast at the general practice after repositioning and was subsequently seen in the hospital 3 times for a fracture check-up. Since the introduction of teleradiology a patient with such a fracture is seen in the hospital once and seen at the general practice twice. In case of other fractures than a wrist fracture the amount of consults before and after 2007 remain the same.

General practitioner

Out of the 426 x-ray examinations 387 were done during the day and 39 at night or on the weekend. 11 Patients were seen in relation to wrist fractures. The income generated by teleradiology were €46,698. The financing costs amount to €16,800; the

operational costs to €28,918. De total cost was €45,718. This lead to a positive balance of €980 for the family doctor (investor) (table 1).

Table 1. Costs and benefits of teleradiology for general practitioner (investor) in 2009

part	revenue	expenditure	balance
426 x-rays	46500		
11x2 extra consuls	198		
maintenance costs		15918	
glass fibre cable costs		7500	
depreciation in 10 years		14000	
10 year loan with 5% interest rate		2800	
radiation measurements of safety		2500	
salary laboratory employee		3000	
total	46698	45718	
positive balance			980

Patients

In 2009 28 out of 426 patients were still referred to the hospital; 398 patients were saved a trip to the hospital for a whole year. Thus the 'Travel cost method' showed a €111,068 savings. The patients and their companions saved €32,388 in travel expenses and €78,680 expenses related to their time loss. Without the use of teleradiology it would have been €111,068 / 398 = €280 more expensive for a patient (table 2).

The estimated savings for a comparable general practice on the main land are much lower, but still significant. Assuming that the travel and hospital time is reduced by half, the estimated savings for this patient are €32,579, an average of €117 per patient.

Table 2. Estimated savings for patients by teleradiology calculated for the general practice on Ameland and for a general practice on the main land

part	GP Ameland	GP main land
x-rays; n	426	
saved trips to hospital total	398	
islanders	278	278
non-islanders	120	
saved time in hours per patient*	8	4
saved reveneus in euro's		
net income per hour actively employed †	15	15
value pensioners ‡	7.50	7.50
value students ‡	2.50	2.50
saved amount of kilometers*	41	41
tariff in euro's /km §	0.40	0.40
saved travel expenses in euro's ||		
islander		
car	39.50	
passenger	5.30	
non-islander		
car	74.80	
passenger	11.45	
estimated savings patients and companions in euro's		
travel expenses	32,388	4,559
time loss	78,680	28,020
total savings in euro's	111,068	32,579
average savings in euro/patient	280	117

* Saved time is determined based on '*ANWB routeplanner'*.

† Net income calculated based on date from Eurostat (www.epp.eurostat.ec.europa.eu)

‡ Estimate based on own assumptions.

§ Kilometer tariff based on date from Nibud (www.nibud.nl/uitgave/huishouden/auto.html).

|| Travel expenses based on Wagenborg Passagiersdiensten ferryboat fares (www.wpd.nl).

Health insuramce companies

Tables 3a-3c show the results for health insurance companies. The patients with fractures in these tables are patients who were immediately eligible for x-ray examination after clinical examinations or according to the *NHG*-standard. Patients with distortions or with trauma symptoms who did not meet the x-ray examination criteria, but whose complaints persisted did still undergo an x-ray examination after a few days. We counted these patients as trauma patients with the corresponding *dbc.*

The cost for the 426 x-ray examinations on Ameland was made up of the reimbursement to the general practitioner for the taken x-ray (€46,700), the radiologist's fee (€4330) and the *dbc's* for referred patients (€23,640); the total cost amounted to €74,670 (see table 3a). The cost without use of teleradiology would have consisted of the radiology claims (€22,103), the specialists costs for patients referred to the specialist (€141,832), in other words the *dbc's* minus the radiology tariff, which amounts to a total €163,935 (see table 3b). The difference of €89,265 (see table 3c) is the estimated saving for the health insurance companies.

Table 3a. Costs health insurance companies with teleradiology

Description	number	Ameland	honorarium radiologist	radio-logist	trauma	referring	DBC surgeon	surgeon	with tele-radiology
	[1]	[2]=[1]*100	[3]	[4]=[1]*[3]	[5]	[6]	[7]	[8]=[5]*([7]-[3])	[9]=[2]+[4]+[8]
L08: shoulder symptoms/complaints	6	600	9.50	57	4	0	547.70	0	657
L09: arm symptoms/complaints	2	200	19.00	38	2	0	547.70	0	238
L10: elbow symptoms/complaints	1	100	5.70	6	1	0	547.70	0	106
L11: wrists symptoms/complaints	2	200	5.70	11	2	0	547.70	0	211
L12: hand/finger symptoms/ complaints	6	600	19.00	114	3	0	316.90	0	714
L13:upper thigh bone symptoms/ complaints	9	900	9.50	86	2	1	2,990.70	2,981	3,967
L15: knee symptom/complaints	6	600	5.70	34	1	1	547.70	542	1176
L16: ankle symptom/complaints	1	100	5.70	6	1	0	547.70	0	106
L17: foot/toe symptom/complaints	6	600	19.00	114	5	0	316.90	0	714
L72: fracture radius/ulna	54	5,400	5.70	308	52	11	547.70	5,962	11,670
L73: fracture tibia/fibula	30	3,000	5.70	171	29	3	547.70	1,626	4,797
L74: fracture hand/foot	47	4,700	19.00	893	46	3	398.10	1,137	6,730
L75: fracture femur	4	400	5.70	23	4	1	2,990.70	2,985	3,408
L76.03: fracture clavicular	7	700	9.50	67	7	0	547.70	0	767
L76.04: fracture humerus	17	1,700	9.50	162	16	3	547.70	1615	3,476
L76.05: fracture rib	1	100	9.50	10	1	0	547.70	0	110
L76.06: fracture spine	8	800	28.50	228	6	1	2,990.70	2,962	3,990
L76.07: fracture pelvis	5	500	9.50	48	5	1	2,990.10	2,981	3,528
L76.08: fracture patella	1	100	5.70	6	1	0	547.70	0	106
L77: distortion ankle	16	1,600	5.70	91	16	1	316.90	311	2,002
L78: distortion knee	3	300	5.70	17	3	0	316.90	0	317
L79: other distortion	25	2,500	9.50	238	25	0	316.90	0	2,738
L80: luxation/subluxation	9	900	9.50	86	9	1	547.70	538	1,524
subtotal *	266	30,700		2,810	241	27		23,640	57,150
X-rays non traumas**	160	16,000	9.50	1,520		8	p.m.		17,444
all x-rays***	426	46,700		4,330		35		23,640	74,670

Source: GP practice Ameland, De Friesland health insurance company and NZA.

The numbers in square brackets indicate column numbers and calculations.

* In de table is calculated with an X-ray fee of 100 euro. The actual fee is calculated in the row Subtotal.

** Radiology costs of 7 control patients of a specialist and one patient referred to the specialist (8 in total) are included in column [9].

*** Additional visits to the GP are included in column [2].

Table 3b. Costs health insurance companies without teleradiology

Description	number	trauma	tariff radiology	radiology	DBCsurgeon	surgeon	without teleradiology
	[1]	[2]	[3]	[4]=[1]*[3]	[5]	[6]=[2]*([5]-[3])	[7]=[4]+[6]
L08: shoulder symptoms/complaints	6	4	52.20	313.20	547.70	1,982.00	2,295
L09: arm symptoms/complaints	2	2	61.70	123.40	547.70	972.00	1,095
L10: elbow symptoms/complaints	1	1	48.40	48.40	547.70	499.30	548
L11: wrists symptoms/complaints	2	2	48.40	96.80	547.70	998.60	1,095
L12: hand/finger symptoms/complaints	6	3	61.70	370.20	316.90	765.60	1,136
L13:upper thigh bone symptoms/complaints	9	2	52.20	469.80	2,990.70	5,877.00	6,347
L15: knee symptom/complaints	6	1	48.40	290.40	547.70	499.30	790
L16: ankle symptom/complaints	1	1	48.40	48.40	547.70	499.30	548
L17: foot/toe symptom/complaints	6	5	61.70	370.20	316.90	1,276.00	1646
L72: fracture radius/ulna	54	52	48.40	2,613.60	547.70	25,963.60	28,577
L73: fracture tibia/fibula	30	29	48.40	1,452.00	547.70	14,479.70	15,932
L74: fracture hand/foot	47	46	61.70	2,899.90	398.10	15,474.40	18,374
L75: fracture femur	4	4	48.40	193.60	2,990.70	11,769.20	11,963
L76.03: fracture clavicular	7	7	52.20	365.40	547.70	3,468.50	3,834
L76.04: fracture humerus	17	16	52.20	887.40	547.70	7,928.00	8,815
L76.05: fracture rib	1	1	52.20	52.20	547.70	495.50	548
L76.06: fracture spine	8	6	71.20	569.60	2,990.70	17,517.00	18,087
L76.07: fracture pelvis	5	5	52.20	261.00	2,990.10	14,689.50	14,951
L76.08: fracture patella	1	1	48.40	48.40	547.70	499.30	548
L77: distortion ankle	16	16	48.40	774.40	316.90	4,296.00	5,070
L78: distortion knee	3	3	48.40	145.20	316.90	805.50	951
L79: other distortion	25	25	52.20	1,305.00	316.90	6,617.50	7,923
L80: luxation/subluxation	9	9	52.20	469.80	547.70	4,459.50	4,929
subtotal	266	241		14168		141,832	156,001
X-rays non traumas*	160		52.20	7934	p.m.	p.m.	7,934
all x-rays	426			22,103		141,832	163,935

Notes. Source: GP practice Ameland and NZA. The numbers in square brackets indicate column numbers and calculations.

* Radiology costs of 7 control patients of a specialist and one patient referred to the specialist (8 in total) are included in column [3].

Table 3c. Savings health insurance companies

Description	with teleradiology	without teleradiology	savings
L08: shoulder symptoms/complaints	657	2,295	1,638
L09: arm symptoms/complaints	238	1,095	857
L10: elbow symptoms/complaints	106	548	442
L11: wrists symptoms/complaints	211	1,095	884
L12: hand/finger symptoms/complaints	714	1,136	422
L13:upper thigh bone symptoms/complaints	3,967	6,347	2,380
L15: knee symptom/complaints	1,176	790	-387
L16: ankle symptom/complaints	106	548	442
L17: foot/toe symptom/complaints	714	1,646	932
L72: fracture radius/ulna	11,670	28,577	16,907
L73: fracture tibia/fibula	4,797	15,932	11,135
L74: fracture hand/foot	6,730	18,374	11,644
L75: fracture femur	3,408	11,963	8,555
L76.03: fracture clavicular	767	3,834	3,067
L76.04: fracture humerus	3,476	8,815	5,339
L76.05: fracture rib	110	548	438
L76.06: fracture spine	3,990	18,087	14,096
L76.07: fracture pelvis	3,528	14,951	11,422
L76.08: fracture patella	106	548	442
L77: distortion ankle	2,002	5,070	3,068
L78: distortion knee	317	951	634
L79: other distortion	2,738	7,923	5,185
L80: luxation/subluxation	1,524	4,929	3,406
subtotal *	57,150	156,001	98,850
X-rays non traumas**	17,444	7,934	-9,510
all x-rays***	74,670	163,935	89,265

Sources: See Table 3a and 3 b

Discussion

This cost-benefit analysis shows that the introduction of teleradiology on Ameland has a beneficial effect on patients and health insurance companies and is almost cost-neutral for the general practitioner (investor). The calculated savings for the health insurance companies can be derived from the fact that teleradiology provides a better selection of patients that need to be referred with more treatments in the general practice as a result. For want of factual financial information we calculated the savings for the health insurance companies by connecting the primary care

registration system (ICPC) to the secondary claim system (*dbc*), these are 2 systems that do not compliment each other well. The savings for the health insurance companies concern an underestimation caused by the fact that the *dbc* cost estimate assumes the cheapest alternative; possibly hospitals make higher claims [8]. Also, extra costs as a result of complications during transportation (decubitus, urinary tract infection) and due to special transportation to the hospital are not considered in the cost estimate.

We consciously chose a theoretical control group (patients who would have had to go to the hospital without teleradiology) in this research instead of comparing patients before and after the introduction of teleradiology. Teleradiology has a great impact on medical decisions. These effects will be elaborately described in an article on the medical-technical consequences of the introduction of teleradiology in general practices.

Finally, this research is based on 1 general practice with specific characteristics (located on a Dutch *Wadden*-island with a large tourist population). When ER's of peripheral hospitals partially or even completely disappear, more areas at great distances from hospitals comparable to Ameland will come into being. Teleradiology is particularly suited in this case as a means to transfer secondary diagnosis and care to primary care providers, with cost reductions in health care as a result.

Conclusion

This study shows that both patients and health insurance companies benefit from the introduction of teleradiology in a family practice on Ameland.

Teleradiology can make a positive contribution to reducing the costs in health care.

References

1. Heijden van der JP, Keizer de NF, Bos JD, Spuls PI, Witkamp L. **Teledermatology applied following patient selection by general practitioner in daily practice improves efficiency and quality of care at lower costs.** *Br J Dermatol* 2011; **165**: 1058-65.
2. Knop FK, Staunting JA. **The benefits of diagnostic imaging in general practice**. *Ugeskr Laeger* 2006;**2**:794-8.
3. Krestin GP, Pieterman H. **Teleradiologie: bedreigingen en kansen. [Teleradiology: threats and opportunities].** *Ned Tijdschr Geneesk* 2011; **155**: A2997. (Dutch)
4. Mun SK, Tohne WG, Platenberg RC, Choi I. **Teleradiology and emerging business models.** *J Telemed Telecare* 2005;**11**(6):271-5
5. Dávalos ME, French MT, Burdick AE, Simmons SC. **Economic evaluation of telemedicine: review of the literature and research guidelines for benefit-cost analyses.** *Telemedicine and e-Health 2009*; **15**(10):933-948.
6. Clarke, Philip M. **Cost–benefit analysis and mammographic screening: a travel cost approach.** *Journal of Health Economics* 1998; **17;** 767-787.
7. Havorsen PA, Kristiansen IS. **Radiology services for remote communities: cost minimisation study of telemedicine.** *BMJ* 1996;**312**:1333-6.
8. Hasaart F. **Incentives in the Diagnosis Treatment Combination payment system for specialist medical care. A study about behavioral responses of medical specialists and hospitals in the Netherlands**. PhD thesis, University of Maastricht 2011.(Dutch)

Chapter 7

Patient satisfaction with a teleradiology service in general practice

Jac. J.W.M. Jacobs, Rianne C.A.M. Ekkelboom, Jan P.A.M. Jacobs, Thys van der Molen and Robbert Sanderman

BMC Fam Pract 2016 Feb 10;17(1):17. doi: 10.1186/s12875-016-0418-y.

Abstract

Background: Accessibility to secondary health services is not always easy for patients who live at a great distance of hospital. In these circumstances, transferring diagnostic tools and treatment options to primary care could prove beneficial for patients. To do so, the quality of medical care and the costs and benefits of the approach need to be assessed. However, the patient perspective is equally important, offering important insights.

Aim: To investigate the satisfaction of patients toward a new teleradiology facility offered in primary care in an island community.

Methods: In a cross-sectional study we investigate the satisfaction of patients toward a new teleradiology facility offered a general practice on Ameland, an island in the Netherlands.
A questionnaire was created based on the Dutch version of the Patient Satisfaction Questionnaire III and completed by all patients after receiving an x-ray in primary care between June 1, 2007 and June 1, 2009. Those who received more than one x-ray in that period were included only once. The technical and interpersonal skills of doctors were rated out the sum score of the questionnaire namely 25 and 30, respectively. Analysis of variance (ANOVA) was used to analyze the differences between the means of the satisfaction subscales and the patient characteristics.

Results: The response proportion was after reminder 65% (381/587 patients). Satisfaction with the technical skills of the doctor providing the teleradiology service was 22.4 ± 3.7, while satisfaction with the interpersonal skills of the doctor during the diagnostic phase was 26.8 ± 3.8. Island residents, the elderly, and those with no history of trauma were more satisfied with the technical and interpersonal aspects of the consultation than non-residents, younger patients, and those with a history of trauma.

Conclusion: Patients in the island community of Ameland experienced high levels of satisfaction with the teleradiology service offered in primary care.

Background

The debate as to whether traditional secondary care services can be transferred to primary care has received renewed impetus, not only because of the need to control spiraling healthcare costs [1,2,3] but also because of developments in the available technology [4,5,6,7,8]. Indeed, it is now possible for the general practitioner (GP) and the specialist to discuss and determine treatment options through the exchange of electronic data files. Therefore, patients do not necessarily have to attend hospital for specialist diagnostic assessment. This approach is, already commonplace in cardiology and dermatology in the Netherlands where electrocardiograms and images of skin abnormalities, respectively, are sent digitally from the GP to the specialist for diagnosis and treatment [9,10]. Another potential area where traditional secondary care services can be introduced to primary care is radiological examination. Teleradiology can be of particular benefit in remote areas.

The present article deals with patient satisfaction of the x-ray and teleradiology service offered in primary care on the Dutch island of Ameland. We showed already that the introduction of teleradiology in general practice has reduced the costs for both the healthcare provider and the patient [11], the number of missed fractures, the unnecessary travel to the hospital with an increase of the treatment in the general practice of normally hospital patients [12]. Given these outcomes it is also very important to investigate whether the patients appreciate such a teleradiology facility. To be particular, the aim of this article is to investigate the satisfaction of patients toward a new teleradiology facility offered in primary care in an island community.

Literature on the use of teleradiology in primary care is scarce [4,5,6,7,8], and to our knowledge only one study has reported the views of patients: a General Practice in Otta, Norway, communicates via teleradiology with the hospital in Lillehammer at a distance of 115 km [7]. Of note, a majority of patients (90%) preferred an x-ray examination in Otta; only 3 % preferred an examination in Lillehammer. Patient satisfaction surveys have been used far more often in the study of telemedicine [13,14,15,16], particularly in the form of teledermatology [17,18,19] and teleconsultation [20]. Again, these studies report very high levels of patient satisfaction with the service [17, 18, 19, 20, 21].

It is known from family practice surveys that the continuity of the doctor-patient relationship affects patient satisfaction, as do various sociodemographic factors such as age, sex, education level, and whether or not the patient is seen by their usual doctor [22, 23, 24, 25]. This is where teleradiology may be perceived as most useful by patients, with the GP able to offer diagnostic procedures and treatment without the need for time-consuming referrals to hospital. Assessment should ideally not only

include the general levels of satisfaction with the service but also the satisfaction with aspects related to the doctor-patient relationship (the interpersonal aspects of care) and the technical skills of GPs providing the service.

Methods

Study design and data collection

We conducted a cross-sectional survey to analyze patient satisfaction with the teleradiology service between June 1, 2007 and June 1, 2009. All patients who had an x-ray in primary care during the study period were included. Those who received more than one x-ray in that period were included only once. Patients or their representatives (eg. of children and patients with dementia) were asked to provide informed consent after making the x-ray on the general practice. After informed consent, a few weeks later a questionnaire was sent to their home addresses and was filled in at home by the patient themselves or by their representatives. The completed questionnaires were returned in pre-paid envelopes to an independent researcher. This procedure was used to guarantee patient anonymity and to limit the potential for response bias. A reminder was sent after three months to all patients. Patients who did not agree with the informed consent did not receive a questionnaire and were excluded. The subscales of the questionnaire that were not completely filled in by the patients were also excluded.

Setting

Ameland is a Dutch island with a population of 3500 inhabitants that increases twenty-fold with an influx of tourists during the peak season. There are only two general practices on the island, with the nearest hospital being located on the mainland, requiring a minimum travel time of four hours. Therefore, a teleradiology service was developed, with the facilities located in one of the general practices, but with the service accessible to all patients regardless of practice or tourist status.

X-rays are taken at the facility by a certified radiographer and digitally transmitted to the mainland hospital in Dokkum where evaluation and interpretation are performed by a radiologist or surgeon. This expert review service is available 24 hours a day for emergencies and during daytime working hours for routine imaging. Moreover, the radiologist always responds the same day and, if necessary, direct by phone with additional instructions for the radiographer. The teleradiology service is indicated for trauma (e.g., fractures) and non-trauma (e.g., hip, knee, or lung imaging) in preparation for surgery (e.g. coxarthrosis) or for monitoring pulmonary pathology (e.g., lung carcinoma).

Quality assurance is maintained through continuous feedback about the quality of x-rays by the radiologist, and by the radiographer receiving a training in the hospital once every three months. The GP is also trained as a radiation protection expert and is responsible for radiation hygiene and safety together with the institute of Nuclear Services for Energy, Environment, and Health in the Netherlands.

Questionnaire

Initially, information on the following variables was collected: sociodemographic variables (included age, sex, educational level, whether or not paid profession, health status, and status as an islander or tourist), previous x-ray experience, treatment experience after the x-ray examination (whether or not the patient received treatment as well as whether that treatment was received in general practice, by the GP or in hospital, by the specialist) and health status. The survey instrument was based on the Dutch version of the Patient Satisfaction Questionnaire III (PSQ.NL), a reliable instrument with adequate validity in hospital settings (e.g., oncology, surgery, cardiology departments) [27]. The PSQ.NL measures, in contrast to the original PSQ, satisfaction in general, as well as satisfaction with the technical quality of the GPs, interpersonal skills, and accessibility of care. However, our focus was on satisfaction with the technical and interpersonal skills of the GP as well as overall satisfaction with the service.

We selected one general satisfaction question, five medical technical questions and six interpersonal questions, beginning with PSQ questions were directly usable without adaptation, and then the ones that were usable with a slight modification. The general satisfaction question (1) was specifically adapted to address the x-ray service instead of the medical care. Two questions (8: I would rather go to the hospital for an x-ray and 12: Taking x-rays is a task for the hospital) replaced the original PSQ question (7: I think my doctor's office has everything needed to provide complete care.; and we added the brand new question 2: I could choose whether to get an x-ray in the GP surgery or in hospital) (Appendix 1). Our questionnaire is completed with four mirror questions (Appendix 2).

The questions were answered using a 5-point Likert scale (i.e., [strongly] disagree, neutral, and agree [strongly]) and a no-opinion possibility. Answers in this last category were excluded from the statistical analyses.

To investigate possible biases in answering the questionnaire questions, we applied the matched pair method using four questions and their mirror questions. The question and mirror questions had opposite ends. Answers to negatively posed PSQ-questions were re-coded on a positive scale such that a high score corresponded to a

positive attitude. A principal component analysis on the answers of the questions with a orthogonal rotation (varimax) with Kaiser normalization, revealed that the medical technical and interpersonal subscales were loaded in the right factors with Cronbach's alfas of 0.76 each.

In addition, the benefits of the service were listed and patients were asked to rate each benefit in terms of its value to themselves (Appendix 3).

Statistical analysis

All analyses were performed with IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA). To determine the representativeness of the sample, age, sex, and island residency (yes or no) were compared with the research population, i.e., all patients that had an x-ray on the island during the research period, between June 1, 2007 and June 1, 2009. Data were presented as means of the sums of the sub-scale questions and standard deviations or as number (percentage). Analysis of variance (ANOVA) was used to analyze the differences between the means of the satisfaction subscales and the patient characteristics.

Results

Respondent characteristics

Of the 587 patients invited to participate in the study, 381 returned the questionnaire (response proportion 65%). The characteristics of the respondents are summarized in Table 1. The youngest patient was 5 years old and the oldest 101 years. The majority of patients (69%) were island residents, with 31% being non-islanders, these as well as gender and age were consistent with the ratios of all patients that had an x-ray on the island during the research period, between June 1, 2007 and June 1, 2009.

Table 1. Characteristics of respondents

Total		Respondents	Total
		381 (65%)	587 (100 %)
1. Sex	Female	206 (54.1%)	(52.1 %)
	Male	170 (44.6%)	(47.3 %)
	No response	5 (1.3%)	(0.7 %)
2. Age	< 20 y	100 (26.2%)	(28.7 %)
	20–60 y	126 (33.1%)	(31.7 %)
	> 60 y	155 (40.7%)	(39.6 %)
3. Islander:	Registered own GP (Ballum)	230 (60.4%)	(68.4%)
	Not registered own GP (Nes)	33 (8.6%)	
	Non-islander	117 (30.7%)	(31.6 %)
	No response	1 (0.3%)	
4. Occupation	Full or part time work	124 (32.5%)	
	Student	98 (25.7%)	
	Summer work	6 (1.6%)	
	Housekeeping	16 (12.1%)	
	Retirement	91 (23.9%)	
	Voluntary	4 (1.0%)	
	Others	4 (1.0%)	
	No response	8 (2.1%)	
5. Education	Primary school	80 (21.4%)	
	GCSE*	168 (45%)	
	A level	38 (10.2%)	
	University	4 (1.1%)	
	Others	83 (22.3%)	
	No response	8 (2.1%)	
6. Earlier x-ray examination.	Yes	301 (89.1%)	
	No	75 (14.2%)	
	No response	5 (1.3%)	
7. When question 6 is answered with yes. When was the examination?	< 3 years ago	154 (40.4%)	
	3–5 years ago	54 (15.2%)	
	> 5 years ago	93 (24.7%)	
8. When question 6 is answered with yes. What was the indication of the x-ray?	Fracture	108 (35.3%)	
	Arthrosis	81 (26.5%)	
	Control specialist	29 (9.5%)	
	Lung pathology	41 (13.4%)	
	Others	43 (14.1%)	
	Unknown	4 (1.3%)	
9. Respondent has paid employment	Yes	122 (34.3%)	
	No	244 (64.0%)	
	No response	5 (1.3%)	
10. Respondent health rating	Excellent	54 (14.2%)	
	Very good	84 (22.2%)	
	Good	178 (46.7%)	
	Moderate	53 (13.9%)	
	Bad	4 (1.0%)	
	No response	8 (2.1%)	

* GCSE, General Certificate of Secondary Education

Most patients were educated to at least secondary school level and were not in paid employment. The main indication for x-ray was suspected fracture (35.3%). The majority (89.0%) had previously had an x-ray examination.

Patient satisfaction

The majority of patients (90.0%) were very satisfied with the general practice teleradiology facility and with the extra medical care they received, scoring ≥ 4 on question 1 (Appendix 4). The preferred arguments in favor of teleradiology were: "I liked the fact that I could stay on the island or at home" (83%); "It took me no travel time" (68%); and "This runs more quickly than in the hospital" (67%) (Appendix 5). Satisfaction with the technical skills of the doctor providing the teleradiology service was 22.4 ± 3.7 and satisfaction with the interpersonal manner of the doctor was 26.8 ± 3.8, out of maximum scores of 25 and 30, respectively (Table 2).

Table 2. Patient satisfaction

Questionnaire: Subscales	Subscales Mean ± SD	number of observations	95% Confidence interval Lower–Upper	Number of items	Cronbach's alpha
Satisfaction about interpersonal manner	26.8 ± 3.8	345	26.4–27.2	6	0.764
Satisfaction about technical quality	22.4 ± 3.7	355	22.0–22.7	5	0.761

Table 3. Patient satisfaction by sociodemographic variables

		Satisfaction with interpersonal manner			Satisfaction with technical quality		
		Mean ± SD	**n**	**ANOVA**	**Mean ± SD**	**n**	**ANOVA**
Total		26.4 ± 3.9	345		22.4 ± 3.7	355	
Sex	**Female**	26.6 ± 3.6	183	0.563	22.6 ± 3.4	189	0.247
	Male	26.9 ± 4.1	157		22.1 ± 4.1	161	
Age	**< 20 y**	24.6 ± 4.7	93	< 0.001	21.5 ± 3.7	96	0.002
	20–60 y	27.1 ± 3.0	116		22.1 ± 4.2	121	
	> 60 y	28.1 ± 3.0	136		23.2 ± 3.3	138	
Islander	**Yes [Registered own GP]**	27.7 ± 3.1 [27.7]	237	< 0.001 [0.845]	23.0 ± 3.2 [23.0]	244	< 0.001 [0.982]
	[Not registered own GP]	[27.6]			[23.0]		
	No	24.9 ± 4.5	108		20.9 ± 4.3	111	
Employment	**Paid**	26.7 ± 3.0	118	0.972	22.3 ± 3.8	125	0.812
	Unpaid	26.7 ± 4.2	222		22.5 ± 3.8	225	
X-ray history	Yes	26.9 ± 3.6	264	0.162	22.4 ± 3.7	264	0.447
	No	26.2 ± 4.7	67		22.1 ± 3.5	67	
X-ray indication:	**Yes**	25.9 ± 4.2	177	< 0.001	21.8 ± 3.9	182	0.004
Trauma	**No**	27.7 ± 3.1	168		22.9. ± 3.5	173	
Treatment	Yes	26.7 ± 3.8	215	0.837	22.2 ± 4.0	221	0.331
	No	27.0 ± 3.9	130		22.6 ± 3.2	134	
Treatment location	**General Practice**	26.8 ± 3.8	128	0.448	22.5 ± 3.6	130	0.141
	Hospital	26.3 ± 3.8	79		21.6 ± 4.5	83	
Health status	**Good**	27.7 ± 3.8	290	0.069	22.3 ± 3.7	304	0.715
	Moderate	26.6 ± 3.9	51		22.6 ± 3.8	55	
Education level	**Low**	27.9 ± 3.9	72	0.155	22.8 ± 3.3	74	0.461
	Medium	27.0 ± 3.0	154		22.5 ± 4.2	157	
	High	26.7 ± 3.0	33		22.5 ± 3.5	33	

Table 3 shows the satisfaction subscales by patient characteristics. ANOVA outcomes indicated a significant difference ($p < 0.001$) for islander patients and non-islander patients on both scales. Differences in satisfaction did not exist by sex, whether patients had previously had an x-ray, whether patients received treatment, whether that treatment was in general practice or hospital, level of education, health status, occupation, or between the two island general practices ($p > 0.05$ for all). However, satisfaction with interpersonal skills was significantly different for several variables ($p < 0.001$), with greater satisfaction for non-traumatic indications (versus traumatic indications), among islanders (versus non-islanders), and with advancing age (over 60 years > 20–60 years > less than 20 years).

Discussion

This study shows that the majority of patients (90%) having an x-ray taken in primary care on Ameland were very satisfied with the service overall and welcomed its introduction. Moreover, satisfaction with both the technical quality and the interpersonal manner were also very high, with neither sex, health status, level of education, previous in-hospital x-ray nor treatment by the GP influencing satisfaction. Island residents were more satisfied than non-residents with both the technical and interpersonal aspects of the service. Thus, the teleradiology service offered in primary care was well received on the Dutch island of Ameland. We believe that, because of the near complete isolation of the population of Ameland, the service facilitated continuity of the doctor-patient relationship for island residents. However, it was clear that the ability to stay on the island was the most important argument in favor of teleradiology, regardless of whether the patient was an islander or not.

Elderly patients and those with non-trauma indications were also more satisfied than younger patients and those with a trauma indication. Although this was true of both satisfaction subscales, the effect was most pronounced on the interpersonal scale for both age and indication. A possible explanation for the different satisfaction outcomes between trauma and non-trauma patients might be the different approach of the GP to the patient. For patients with trauma, the service tends to be more hurried and formal: to ensure accuracy and prevent complications, the GP focus is on providing quick instructions and checks followed by action and conclusion before terminating the consultation. This is a non-standard consultation technique in general practice. In contrast, a session with a non-trauma patient tends to begin with an introduction and then action, which is part of the normal GP-patient conversation that forms the basis of the doctor-patient relationship.

Our findings may be generalizable to other general practices since the current political strategy of the Western governments is to close hospitals, especially in the periphery. This implies that more and more patients will live in the future at a greater distance from the hospital and general practices becoming more remote. Our findings will be relevant for these remote general practices.

Strengths and limitations

This is the largest study of patient satisfaction with teleradiology in primary care, adding additional information to our existing knowledge base in this area. In addition, it is the first study that investigates patient satisfaction in general and the technical quality and interpersonal manner during their experience of the teleradiology service. Another notable strength is the response proportion of 65%.

Limitations of the study are the cross sectional design, it is a study at on specific point in time and we do not know the level of patient satisfaction before the introduction of the teleradiology service. Satisfaction with referral to the mainland hospital for an x-ray is also unknown. Both these facts preclude meaningful comparison. Therefore, we cannot conclude whether patient satisfaction improved after the introduction of the teleradiology service, or whether there was truly greater satisfaction than with the usual hospital service. Nevertheless, the most important perceived benefit with the teleradiology service in the general practice was the fact that patients could stay on the island. Future studies in this area might benefit from a before and after comparison to confirm our argument.

A further limitation is, the questionnaire is not completed directly after the x-ray is taken but after a short period which can – in theory - provide a bias. Also the fact that a validated questionnaire did not exist, so that we had to adapt the original PSQ-NL questionnaire is a limitation as well as the relatively high percentage of patients not answering certain items.

Another limitation is the concept of satisfaction. It is known that surveys of patients' satisfaction often fail to distinguish between individual doctors because most of the variation in doctors is due to differences between patients and random error rather than differences between doctors. Measures related to patients' experience discriminate more effectively between practices than do measures of general satisfaction [28]. However when we started our study the Consumer Quality (CQ) - questionnaire was not yet sufficiently developed [29].

Comparison with existing literature

As mentioned in the background, we found just one article concerning teleradiology and patient satisfaction in general practice. However, that study did not distinguish

between different subscales of satisfaction. The article concluded that patients were satisfied with the new facility and particularly appreciated the facility nearby [7]. This is consistent to our finding that, when using the teleradiology service, patients preferred the ability to remain on the island, the short travel time, and the faster service time in comparison with the hospital service.

In contrast to the limited research into patient satisfaction of teleradiology in primary care, more research has been performed into patient satisfaction of telemedicine in general [13,14, 15, 16, 20] and teledermatology in particular [17, 18, 19]. Nevertheless, each of these studies are deficient in some way, having small samples, low response rates, short investigation periods, or narrow definitions of satisfaction [18, 20]. Our study resolves these issues, providing a large sample with an acceptable response proportion over a long investigation period, while using clear definitions and measures of satisfaction.

It is well known from patient satisfaction studies of GPs that age, being seen by the same or usual doctor, education, sex, and health status can affect satisfaction with interpersonal communication [22, 23, 24, 25, 26]. In our study, we additionally identified that satisfaction was different for technical quality and interpersonal manner. Indeed, satisfaction with the interpersonal manner was strongly affected by the patients' age, whether they were an islander, and the indication for x-ray (trauma or not), while satisfaction with the technical quality was also strongly affected by whether they were an islander or not, but was less strongly influenced by age or indication. This distinction between island and non-island residents does not exist in the literature, which has only distinguished registered patients from others. Our data was also notable for the lack of influence of patient education status, health status, or sex on satisfaction levels, a fact that contrasts with the existing literature on satisfaction with GPs. This may however be an artefact of the specific period for which we carried out our study.

Implications for research and practice

Future research should assess whether our finding that patients appreciate the teleradiology service also holds true for less remote general practices. In addition, more research is needed to assess the influence of the continuity of the doctor-patient relationship on patient satisfaction this together with the development of a patient satisfaction survey focused on the use of hospitals facilities in the general practice. Further research may also benefit from the inclusion of a Consumer Quality Index [29, 30, 31, 32] to advance our understanding of the patient experience.

Conclusion

This study completes our research into the pilot teleradiology service in primary care on the Dutch island of Ameland. The introduction of teleradiology reduced the number of missed fractures and unnecessary referrals to the hospital and led to an increase in fracture treatment by the GP [12]. Moreover, it resulted in considerable cost reductions for patients (111k euro per year) and health insurance companies (minimum 89k euro per year) [11]. This study adds to these results, by showing that patients appreciated the teleradiology service. Thus, we conclude that the teleradiology is a suitable candidate secondary care facility for transfer to primary care, especially for patients who live at a considerable distance from hospital.

Acknowledgements

The authors would like to thank Marina Beckers, for assistance with the logistics of the questionnaire and the first analysis of the outcomes, and the editor for detailed comments and suggestions which improved our manuscript considerably.

References

1. Wistow G. **Decentralisation from acute to home care settings in England.** *Health Policy* 1997 Sep;**41**:suppl 91 -108.
2. Robberts E, Mays N. **Can Primary Care and Community Based Models of Emergency Care substitute for the Hospital Accident and Emergency (A & E) Department?** *Health Policy* 1998 Jun;**44** (3); 191-214.
3. Starfield B, Shi L, **Policy Relevant Determinants of Health: an International Perspective.** *Health Policy* 2002 June; **60** (3): 201-218.
4. Norum J, Pedersen S, Stormer J, Rumpsfeld M, Stormao A, Janissen N, Sunde H, Ingebrigtsen T, Larsen ML. **Prioritisation of Telemedicine Services for Large Scale Implementation in Norway.** *J Telemed Telecare* 2007;**13**:185–192.
5. Ekeland AG, Bowes A, Flottorp S. **Effectiveness of Telemedicine: A Systematic Review of Reviews.** *I J Med Inform* 2010;**79**:736–771.
6. Mun SK, Tohne WG, Platenberg RC, Choi I**. Teleradiology and Emerging Business Models.** *J Telemed Telecare* 2005;**11**(6):271–275.
7. Johansen I. **Experience with Teleradiology in General Practice in Oppland.** *TIdsskr Nor Laegeforen* 2000 Jun 20;**120**(16):1896–1898.
8. Knop FK, Staunting JA. **The Benefits of Diagnostic Imaging in General Practice.** *Ugeskr Laeger*. 2006;**2**:794–8.
9. Backman W, Bendel D, Rakhit R. **The Telecardiology Revolution: Improving the Management of Cardiac Disease in Primary Care.** *J R Soc Med* 2010: **103**: 442-446.
10. Heijden van der JP, Keizer de NF, Bos JD, Spuls PI, Witkamp L. **Teledermatology Applied Following Patient Selection by General Practitioner in Daily Practice Improves Efficiency and Quality of Care at Lower Costs.** *Br J Dermat* 2011;**165**:1058–1065.
11. Jacobs JJWM, Jacobs JPAM, Wiersma D, Sanderman R. **Teleradiology in the General Practice at Ameland: A Benefit Cost Analysis.** *Ned Tijdschr Geneesk* 2013;**156**(51):A5428. (Dutch)
12. Jacobs JJWM, Jacobs JPAM, van Sonderen F, van der Molen T, Sanderman R. **Fracture Diagnostics, Unnecessary Travel and Treatment: A Comparative Study Before and After the Introduction of Teleradiology in a Remote General Practice.** *BMC Fam Pract* 2015 May 6;**16**(1):53.
13. Marshall GN, Hays RD, Sherbourne CD, Wells KB. **The Structure of Patient Satisfaction with Outpatient Medical Care.** *Psychological Assessment* 1993;**5**(4):477–483.

14. Aoki N, Dunn K, Johnson-Throop KA, Turley JP. **Outcomes and Methods in Telemedicine Evaluation.** *Telemed J E Health* 2003;**9**(4);393–401.
15. Whitten P, Love B. Patient and Provider Satisfaction with the Use of Telemedicine: **Overview and Rationale for Cautious Enthusiasm**. *J Postgrad Med* 2005;**51**(4):294–300.
16. Mair F, Whitten P. **Systematic Review of Studies of Patient Satisfaction with Telemedicine.** *BMJ* 2000;**320**:1517–1520.
17. Whited JD, Hall RP, Foy ME, Marbrey LE, Grambow SC, Dudley TK, Datta SK, Simel DL, Oddone EZ. **Patient and Clinician Satisfaction with a Store-And-Forward Teledermatology Consult System.** *Telemed J E Health* 2004;**10**(4):422–431.
18. Whited JD, MD, MHS. **Teledermatology Research Review.** *Int J Dermat* 2006, **45**, 220–229.
19. Demiris G. Speedie SM, Hicks LL. **Assessment of Patients' Acceptance of and Satisfaction with Teledermatology**. *J Med Syst* 2004;**28**(6):575–579.
20. Iseli MA, Kunz R, Blozik E. **Instruments to Assess Patient Satisfaction after Teleconsultation and Triage: A Systematic Review.** *Patient preference and adherence* 2014;**8**:893–907.
21. Grogan S, Norman P, Willits D, Porter I. **Validation of a Questionnaire Measuring Patient Satisfaction with General Practitioner Services.** *Qual Health Care* 2000 Dec;**9**(4):210–215.
22. Rahmquist M, **Patient Satisfaction in Relation to Age, Health Status and other Background Factors: A Model for Comparisons of Care Units.** *Int J Qual Health Care* 2001;**13**(5):385–390.
23. Campbell JL, Ramsay J, Green J. **Age, Sex, Socioeconomic, and Ethnic Differences in Patients' Assessments of Primary Health Care.** *Qual Health Care* 2001;10:90–95.
24. Jung HP, Baerveldt C, Olesen F, Grol R, **Wensing M. Patient Characteristics as Predictors of Primary Health Care Preferences: A Systematic Literature Analysis.** *Health Expect* 2003;**6**:160–181.
25. Howard M, Goertzen J, Hutchison B, Kaczorowski J, Morris K. **Patient Satisfaction with Care for Urgent Health Problems: A Survey of Family Practice Patients.** *Ann Fam Med* 2007 Sep–Oct;**5**(5):419–424.
26. Hankins M, Fraser A, Hodson A, Hooley C, Smith H. **Measuring Patient Satisfaction for the Quality and Outcomes Framework.** *Br J Gen Pract* 2007;**57**:737–740.

27. Hagedoorn M, Uijl SG, Van Sonderen E, Ranchor A, Grol BMF, Otter R, Krol B, Van den Heuvel W, Sanderman R. **Structure and Reliability of Ware's Patient Satisfaction Questionnaire III. Patients' Satisfaction with Oncological Care in the Netherlands.** *Medical Care* 2003;**41**(2):254–263.
28. Salisbury C, Wallace M, Montgomery AA. **Patients 'experience and satisfaction in primary care: secondary analysis using multilevel modelling.** *BMJ* 2010;**341**:c5004.
29. Delnoij D, Ten Asbroek G, Arah O, De Koning J, Stam P, Poll A, Vriens B, Schmidt P, Klazinga N. **Made In USA: The Import of American Consumer Assessment of Health Plan Surveys (CAHPS) into the Dutch Social Insurance System.** *Eur J Public Health* 2006 Dec **16**(6):652–659.
30. Damman OC, Hendriks M, Sixma HJ. **Towards More Patient Centered Healthcare: A New Consumer Quality Index Instrument to Assess Patients' Experiences with Breast Care.** *Eur J Cancer* 45;2009:1569–1577.
31. Berendsen AJ, Groenier KH, De Jong GM, Meyboom-de Jong B, Van der Veen WJ, Dekker J, De Waal MWM, Schuling J. **Assessment of Patient's Experiences across the Interface between Primary and Secondary Care: Consumer Quality Index Continuum of Care.** Patient Education Counseling 77;2009:123–127.
32. Meuwissen LE, De Bakker DH. **Consumer Quality'-Index 'General Practice Care' Measures Patients' Experiences and Compares General Practices with Each Other.** *Ned Tijdschr Geneesk* 2009;**153**:A180. (Dutch)

Appendix 1. Patient satisfaction questions

Modified Questionnaire Item	***Changes from Original Patient Satisfaction Questionnaire III (bracketed number indicates the original PSQ item)***
General Satisfaction	
1. I am very satisfied with the radiology instrument and the additional medical care I receive	***(****3). I am very satisfied with the medical care I receive*
Interpersonal Satisfaction	
2.I could choose whether to get an x-ray in the GP surgery or in Hospital	(*New question)*
3. The GP spends plenty of time with me	*(38) Doctor is replaced by GP*
4. The GP who treats me has a genuine interest in me as a person	*(14) Doctor is replaced by GP*
5. The GP listens carefully to what I have to say	(*36) Doctor is replaced by GP*
6. They did their best to keep me free from worrying	(*39) Doctors always do their best to keep me free from worrying*
7. All things considered, the medical care I receive is excellent	(*35) All things considered, the medical care I receive is excellent*
X-Ray Medical Technical Satisfaction	
8. I would rather go to the hospital for an x-ray	*Newly developed from: (7) I think my doctor's office has everything needed to provide complete care.*
9. The GP makes me wonder if his or her diagnosis is correct	(*10) Doctor is replaced by GP*
10. I have some doubts about the ability of the GP who treats me	(*37)Doctor is replaced by GP*
11. There are some things about the medical care I received that could be better	(*26*) *There are some things about the medical care I receive that could be better*
12. Taking x-rays is a task for the hospital	*Newly developed from: (7) I think my doctor's office has everything needed to provide complete care.*

Appendix 2. Mirror Questions

3. The GP spends plenty of time with me	**13 . Those who provide me medical care hurry too much when he or she treats me**
5 The GP listens carefully to what I have to say	**14. There was no opportunity for me to ask questions**
10 I have some doubts about the ability of the GP who treats me	**15.The doctor who treats me is competent and well-trained in the x-ray examination**
12. Taking x-rays is a task for the hospital	**16. I am pleased with the x-ray facility and the extra treatment**

Appendix 3. Patients' perceptions and expectations

What was important to you when the x-ray was made in the general practice?
I had the result immediately
I was shorter uncertain
I had shorter pain and discomfort
The treatment has been deployed faster
I saved travel costs
It took me no travel time
I lost less spare time
It took me no loss of time or revenues
I liked the fact that I could stay on the island or at home
This runs more quickly than in the hospital
I got the same quality of care as in the hospital
I saved costs

Appendix 4. Results patient satisfaction questions

	strongly agree	agree	neutral	disagree	strongly disagree	no opinion
General Satisfaction						
1. I am very satisfied with the radiology instrument and the additional medical care I receive	80.8%	9.2%	3.4%	1.8%	1.3%	3.4%
Interpersonal Satisfaction						
2. I could choose whether to get an x-ray in the GP surgery or in Hospital	54.3%	6.0%	16.8%	3.1%	13.9%	5.8%
3. The GP spends plenty of time with me	82.4%	8,4%	3.4%	1.0%	0.8%	3.9%
4. The GP who treats me has a genuine interest in me as a person	74.0%	12.3%	6.6%	1.3%	1.3%	4.5%
5. The GP listens carefully to what I have to say	78.0%	11.8%	3.4%	0.8%	1.0%	5.0%
6. They did their best to keep me free from worrying	75.3%	13.9%	5.5%	0,5%	0.8%	3.9%
7. All things considered, the medical care I receive is excellent	46.7%	18.4%	24.1%	1.8%	3.4%	5.5%
X-Ray Medical Technical Satisfaction						
8**. I would rather go to the hospital for an x-ray**	2.6%	4.7%	7.9%	5.5%	75.6%	3.7%
9. The GP makes me wonder if his or her diagnosis is correct	3.4%	4.2%	6.0%	6.3%	74.8%	5.2%
10. I have some doubts about the ability of the GP who treats me	2.6%	0.8%	5.5%	6.0%	80.6%	4.5%
11. There are some things about the medical care I received that could be better	5.2%	7.6%	10.0%	10.0%	63.5%	3.7%
12. Taking x-rays is a task for the hospital	1.8%	6.0%	11.5%	9.7%	66.1%	4.7%

Appendix 5. Results: Patients' perceptions and expectations

What was important to you when the x-ray was made in the general practice?	Very important	Important	Neutral	Not important	Totally not important	No comments
I had the result immediately	164(43%)	88(23%)	38(10%)	4(1%)	11(3%)	76(20%)
I was uncertain for less time	156(41%)	84(22%)	50(13%)	4(1%)	8 (2%)	79(21%)
I had shorter pain and discomfort	114(30%)	76(20%)	69(18%)	8(2%)	11(3%)	103(27%)
The treatment has been deployed faster	141(37%)	84(22%)	42(11%)	11(3%)	8 (2%)	95(25%)
I saved travel costs	149(39%)	76(20%)	49(13%)	15(4%)	46(12%)	46(12%)
It took me no travel time	183(48%)	76(20%)	34(9%)	11(3%)	23(6%)	54(14%)
I lost less spare time	130(34%)	69(18%)	49(13%)	15(4%)	46(12%)	72(19%)
I had no loss of time or revenues	95(25%)	58(15%)	72(19%)	15(4%)	46(12%)	95(25%)
I liked the fact that I could stay on the island or at home	244(64%)	72(19%)	11(3%)	4(1%)	8(2%)	42(11%)
This runs more quickly than in the hospital	168(44%)	88(23%)	31(8%)	4(1%)	11(3%)	79(21%)
I got the same quality of care as in the hospital	160(42%)	88(23%)	46(12%)	4(1%)	8(2%)	76(20%)
I saved costs	103(27%)	69(18%)	61(16%)	15(4%)	15(4%)	118(31%)

Chapter 8

General conclusion and recommendations

Introduction

This thesis describes three specific medical problems with which I was confronted as a general practitioner (GP) on Ameland: ticks, Ameland disease (*Amelander krankheit*), and traumatology. Unfortunately, the management guidelines of the Dutch College of General Practitioners (NHG, *Nederlands Huisartsen Genootschap*) were unsuitable for application in this clinical setting. The guidance on the management of ticks was limited by concerns over their quality, while those for gastroenteritis lacked detail about the etiology of Ameland disease, and those for traumatology were not applicable because they did not allow for the distance to the hospital. Thus, further research was performed and has been discussed in this thesis.

The NHG guidelines for Lyme disease and Ameland disease were lacking. To rectify this, additional epidemiological research was necessary, the results of which were described in Section 1. Concerning traumatology, because the distance to hospital precluded compliance with the guidelines, an innovative approach was used and described in Section 2. In this chapter, we summarize these results and discuss the implications for care provision and future research. Finally,we consider the overarching theme of guideline revision and the implications for research in general practice.

Epidemiological research into Amelander Disease

The cause of Amelander disease

In a large area of Germany, annual gastroenteritis epidemics occurred in children between 1958 and 1995 due to infection with Campylobacter jejuni. Because the symptoms always arose after staying on Ameland, the condition was dubbed Amelander disease (*Amelander Krankheit*). Guidelines produced by the NHG for gastroenteritis were shown to focus on diagnosis and treatment, with inadequate attention given to prevention. Although all potential bacterial sources were required to be assessed and excluded, the source of the *Campylobacter jejuni* often remained a mystery. Given that, further investigation was certainly justified.

Results for Amelander Disease

We have all grown up with the idea that drinking milk is healthy. Despite this, the incidences of Amelander disease and arthritis described in Chapter 2 show that this is not always the case. Today, milk is generally pasteurized or sterilized before human consumption, making it an unlikely disease vector. However, our research suggests that the consumption of raw milk containing the bacterium *Campylobacter jejuni*

was the ultimate cause of the Amelander krankheit.

Care implications for Amelander Disease

The consumption of raw milk is likely to continue in the Netherlands. Cheese farms with educational elements (i.e., for school trips) are common, and continue to offer their visitors raw milk. Our advice is for doctors presented with patients who have gastroenteritis or rheumatic complaints to enquire about a recent history of drinking raw milk, because this could be a possible cause of the symptoms.

Research implications for Ameland Disease

In the nineties the *C.jejuni* was only present in the milk in the east on the island. In 2013 C.*jejuni* had spread in the milk all over the island.For this expansion of the spread, we provide two explanations : first, that during dry summers, the drinking water from cows readily becomes contaminated, which consequently infects their milk; and second, that the *C. jejuni* is transmitted by migratory birds. Further research into how the disease spreads is important.

Epidemiological research into tick-borne disease

The management of tick-borne disease

In the early nineties, around 20% of ticks were known to be infected with the Borrelia bacterium [1]. Animal testing showed that transfer from tick to animal was rare, and occurred only after about 24 hours' exposure [2]. This knowledge, along with the belief that Lyme disease was treatable, formed the basis for the policy that it was safe to wait after a tick bite in humans. Although the transmission risk in animals and humans was unknown, it was assumed to be low. "Tick prevention" was also included in the guidelines of the National Coordination for Communicable Diseases Control in the Netherlands (LCI, *Landelijke Coördinatiestructuur Infectiebestrijding*) [3]. However, GPs had no specific guidelines from the NHG regarding the management of Lyme disease.

Increases in the number of patients with Lyme disease in the Netherlands led to the "wait and see" guidance of the LCI coming under huge scrutiny. Although ticks are present in high numbers on Ameland, there has been no clear increase in the incidence of Lyme disease. Despite this, it is still believed that you have a greater chance of contracting Lyme disease on Ameland. The abundance of ticks in the surrounding area was a major justification for further research on the risk of disease transmission. This also provided an opportunity to increase our knowledge of Lyme disease.

Results of the study into tick-borne disease

In Chapter 3, we showed that the chances of contracting Lyme disease following a tick bite were relatively small if the tick could be removed in time (approximately 1 in a 100), even though 20% of ticks on Ameland have been shown to be contaminated with *Borrelia burgdorferi*. Indeed, the only infected patient in our study had a tick attached on the skin for more than 48 hours. Thus, our findings support the existing treatment guidelines [3] that antibiotics should only be prescribed when clinical symptoms of Lyme borreliosis are manifest, and not following each consult for a tick bite.

In Chapter 4, we highlight that the overall risk of developing clinical symptoms after a tick bite was just 11.4%, and that most of these symptoms were restricted to local reactions. None of the participants in our study developed symptomatic rickettsiosis, babesiosis, or ehrlichiosis. Thus, the risk of overt symptomatic disease after a tick bite was lower than 0.5% in the study population. Although prompt removal of ticks reduces the risk of developing symptoms, the most powerful measures against tick-borne diseases are preventive, including thorough checking for ticks, wearing appropriate clothing, ensuring tick-avoidance behaviors, and using insect repellents.

Care Implications surrounding tick-borne disease

There remains a great deal of uncertainty regarding Lyme disease. There is strong epidemiological evidence that the number of *Borrelia burgdorferi* infections may still be on the increase in the Netherlands. Doctors, including GPs, will increasingly be confronted with queries about the prevention, diagnosis, and treatment of Lyme disease, which will demand greater GP involvement. Poor GP participation, as described in research by the RIVM (*Rijksinstituut voor Volksgezondheid en Milieu*; see 5.2), should not be allowed to happen again.

Patient unions and organizations have criticized the uncertainties and differences of opinion that exist over the diagnosis and treatment of Lyme disease. Under pressure, the government has asked the Citizen Health Council to provide an opinion on Lyme disease, and the government now strongly recommends that all professionals take note of their advice, which is consistent with that of current scientific opinion [4]. Furthermore, the government called for knowledge and expertise to be collected and for a survey to be conducted by two treatment centers. However, this has been limited to medical issues, which has missed the opportunity for greater patient involvement that could resolve limitations with the current approach.

The wait and see approach continues to be the main advice of the NHG when treating patients with a tick bite. However, the guidance also recommends discussing the pros

and cons of antibiotic prophylaxis in cases where the tick has been attached to the skin for more than 24 hours and at any point within 72 hours after removal of the tick. For non-pregnant patients aged eight years or older, a doctor might consider a single preventive dose of 200 mg doxycycline. For pregnant women or children between 6 months and 8 years, a single dose of 500 mg azithromycin can be given (10 mg/kg for children). However, when early local Lyme disease is suspected (e.g., erythema migrans or Borrelia lymfocytoom), antibiotic treatment should be with doxycycline (100 mg, twice daily) for 10 days or, in children and those with contraindications to doxycycline, treatment should be with amoxicillin (50 mg/kg/day in 3 doses) for 14 days or azithromycin(10mg/kg/day in one dose) for 5 days.

Strengths and limitations of the tick study

To the best of our knowledge, our study is the first to link ticks and patients directly. Further strengths are the clearly defined research area and design within general practice (see Chapter 4 for further details). A possible shortcoming of this part of the research is that the patients were interviewed six or more months following the tick bite. Although we chose this to be able to assess the symptoms of Borrelia infection that only manifest after a longer period of time, it is nevertheless possible that patients may have forgotten minor symptoms. It might also have been reasonable to perform additional diagnostic screening (e.g., polymerase chain reaction of a biopsy, or evidence of seroconversion). However, serological follow-up is useless when treatment with antibiotics has already been started, as was the case with four patients in our study, because antibody response will fail to develop in seronegative patients with erythema migrans treated with antibiotics.

Further research into ticks and Lyme disease

Experts predict that, because there has been a migration of ticks to the north, there will be an increase in the amount of ticks in the Netherlands. Climate change and socioeconomic factors play an important role in this and have a considerable influence on the geographic dispersion, population density, and carrier rate among ticks and their hosts [5] including all the risks that accompany this. The GPs throughout the Netherlands will see because of this migration of ticks, more ticks, and more Lyme disease. The burning question is if we are with the current preventative interventions and medical policies properly prepared for the future. A pro-active policy is desired. Many questions in this area remain unanswered, especially in the health care area and the localization of the preferred habitats of ticks.

Medical policy

Currently, 20% of ticks are carriers of infection. Early awareness of whether the tick is infected would therefore be a welcome addition to our current diagnostic options. The hope is that research will become available to develop a quick diagnostic instrument for use in general practice. The current prophylaxis policy (200 mg doxycycline in cases where the tick has been attached to the skin for more than 24 hours and at any point within 72 hours after removal of the tick) also remains insufficiently evaluated, and it is unknown whether this treatment is sufficient to prevent Lyme disease. Indeed, the recommendation is based on just one RCT conducted in the USA [6]. In that research, they not only targeted a different tick (*Ixodes scapularis*) to that which is endemic in the Netherlands (*Ixodes ricinus*) but also targeted a different Borrelia species (*Borrelia Burgdorferi s.s.* in the USA versus *Borrelia Afzelii* in the Netherlands). Given that only one in five tics carry the infection, the implication is that some 80% of antibiotics are probably given in vain. Not only because of the potential for complications but also because of increasing resistance to antibiotics, it is important to be cautious when prescribing doxycycline. Further research is clearly required, and recently the "Tick Test & Prophylaxis Proof"[7] investigation was started with the RIVM in cooperation of two departments of family medicine (University of Amsterdam and Radboud University, Nijmegen).

Localization and prevention

Regarding prevention, the behavior of people is of critical. In future research, it would be good to determine which environments ticks favor so that we can better advise people to avoid them. Currently, there is a sort of "tick radar" system that indicates where most ticks can be found in the Netherlands. It is also known that ticks are most active in environments where the ambient temperature is between 25°C and 27°C, with a humidity level of 45% [8]. Researchers at Wageningen Agricultural University are developing a model that combines temperature, humidity, and environmental variables to predict where ticks can be expected. Such a model could form the basis for an early warning system that, similar to the current red and green risk categories for swimming, extends beyond the simplistic tick radar system.

Research organization

Currently, research into ticks and Lyme disease is being done at institutions with veterinary, agricultural, landscape architecture, and medical perspectives. These efforts may be more effective if combined in a joint multidisciplinary effort, perhaps with the GP taking a coordinating role.

Teleradiology

The management of trauma using teleradiology

Working as a GP on an island requires an understanding of the extent of your professional capabilities, but the distance to hospital can be an obstacle to following best-practice guidelines (e.g., those of the NHG). In situations when time is critical, GPs are often forced to act immediately, and may lack specific skills and additional diagnostic facilities that are sometimes required. To minimize treatment delay and prevent unnecessary hospital attendance, GPs therefore often start diagnosis and treatment when possible and where the risks of treatment are outweighed by the risks of potential non-treatment. Since 1992, electrocardiograms and ultrasound devices have improved such experience in cardiology and obstetrics. In addition, employing a cautious referral policy for fractures, thereby deviating from official guidelines, has reduced the need for patients to attend hospital with no fracture. However, to reduce the risk of missed diagnosis, additional diagnostic facilities were advised, so an x-ray machine was purchased in 2007 and teleradiology has been used to facilitate communication with radiologists and surgeons. Questions remain over this approach, including whether patients accept and appreciate hospital services being delivered by their GP, whether the same standards can be delivered as at hospital, and whether this innovation is cost effective for society.

Results for the teleradiology study

Doctors in remote settings have greater demands on them because of their isolation from modern diagnostic equipment and because of a pressure to manage patients without referral. Thus, the risk of missed diagnosis increases due to the need to avoid unnecessary hospital referral, which would incur unnecessary disruption and cost for patients. This was the situation regarding fracture management prior to 2007 on the relatively remote island of Ameland. To provide a means for GPs to perform radiology and to communicate with hospital-based radiologists and surgeons without the patient needing to attend hospital, an on-site x-ray service was introduced and supplemented by teleradiology. This was expected to reduce the existing referral dilemma and to lower the particularly high threshold for ordering diagnostic imaging.

In Chapter 5, we showed that teleradiology provided clear benefits in terms of reducing the number of missed fractures and increasing the potential for at-home rather than in-hospital treatment. Fewer patients also had to make the unnecessary five-hour trip to hospital. Therefore, teleradiology had important consequences on both diagnosis and treatment, and given that more patients could be treated in general practice, treatment delays were reduced. Although the number of x-rays increased, teleradiology better enabled GPs to comply with the relevant Dutch

guidelines despite their large distance from hospital, particularly for patients with uncertain clinical signs; there were fewer missed fractures and a better quality of care. Teleradiology, in this setting, therefore represented a good example where healthcare can be transferred from hospitals to primary healthcare centers.

In Chapter 6, we showed that the introduction of teleradiology on Ameland resulted in considerable cost reductions for both patients and health insurance companies, but with only a small profit for the investor (in this case the GP). Teleradiology resulted in considerable financial benefits for patients (€111,000 per year) and for health insurance companies (minimum €89,000 per year). The cost increase caused by the increase in the number of x-rays indicated in the NHG guidelines was marginal when compared with the savings in expensive hospital costs.

In Chapter 7, we reported a very high response rate to the patient satisfaction questionnaire, and concluded that the majority of patients (including tourists) who received an x-ray in general practice welcomed the introduction of teleradiology on the island. Satisfaction was also quite high with the technical knowledge of GPs concerning the teleradiology facility and with the interpersonal communication of the doctors and radiographers involved. Island residents were more satisfied than non-residents with both the technical aspects and interpersonal skills related to the service. Elderly patients and those with non-trauma indications were also more satisfied than younger patients and those with a trauma indication. Although this was true of both satisfaction subscales (i.e., technical and interpersonal), the effect was most pronounced on the interpersonal scale for both age and indication. However, the following had no influence on patient satisfaction: sex, health status, education level, in-hospital experience with an x-ray machine and practice-based GP treatment compared with hospital-based specialist treatment. Being able to stay on the island was the most important argument for patients in favor of teleradiology, with two-thirds of the respondents (66%) considering time savings to be very relevant, specifically through reduced travel and faster diagnosis and treatment. Three-quarters of the respondents (75%) agreed that x-rays do not always need to be performed in a hospital.

In summary, the introduction of teleradiology services to general practice in Ameland, an island to the north of the mainland Netherlands, reduced the number of missed fractures and unnecessary hospital referrals and increased the number of fractures treated by GPs. In addition, the introduction of teleradiology was appreciated by patients and resulted in cost savings.

Care implications teleradiology

The Dutch Institute for Health Services Research (*Nederlands Instituut voor*

Onderzoekvan de Gezondheidszorg; NIVEL) has observed that, despite shifting from secondary to primary care being on the policy agenda since 2007, much remains unknown about what could be managed in primary care, and indeed, the effects of such a switch [9]. The teleradiology project highlights that such a process can result in fewer missed diagnoses, fewer patients being referred to hospital for additional diagnostic tests, and more treatment being performed by the GP. Besides these gains, the research also suggests that a considerable cost reduction can be achieved. Given that this project was based on need (distance to hospital), it can be a good example for other rural GP practices. Moreover, it is of particular relevance given current austerity policies and the aim of health insurance companies to increase the role of primary care. In the future, increasing amounts of routine hospital procedures may be performed by GPs, with both the NHG and the LHV (*Landelijke Huisartsen Vereniging*) being strong advocates for such a change and anticipating that capacity could be achieved by 2022.

Furthermore, it is predicted that the need for local GP-led services will be heightened by the increase in distance between general practices and hospitals. Current policies are seeking to centralize specialist care into a limited number of hospitals (including diagnostic facilities) with general practices increasingly becoming located at greater distances from specialist hospitals. Thus, GPs who refer reluctantly might not be able to work within the guidelines and will risk missed diagnoses and a reduction in the quality of care they provide. Greater provision of diagnostic facilities by general practice surgeries could prevent this undesirable situation. Reluctance to refer to hospital is also influenced by the extra costs for patients; as part of their "liability policy," which typically includes hospital care, patients may choose to avoid such care. The first signs of this are evident, and should GPs seek to fill this gap and maintain the quality of care, they will need to provide more secondary care services.

Using teleradiology to diagnose and treat former hospital patients under the supervision of a consultant might also be effective in this context. In practice, a number of conditions must be fulfilled for this care substitution to have a chance of success. For GPs and their assistants, this would require them to have sufficient knowledge and skills at their disposal to provide comparable quality and continuity of care to that offered by hospitals. As NIVEL indicate, there must be mutual trust between consultants and GPs [10,15]. In our teleradiology project, initial reticence by the hospital consultants was replaced by greater involvement over time. For instance, consultants started to ask GPs to take control images of tumors in the surgery before discussing the findings with the patient by telephone.

The support of patients is also equally important. To our knowledge, patient

experience with care substitution between primary and secondary care has not been comprehensively studied in the Netherlands. NIVEL has previously shown fictitious situations to a patient panel, asking them to indicate preference for treatment by a consultant or by a GP. The patients reported confidence that a GP could assess patients for chronic obstructive pulmonary disease, diabetes, and other less complicated conditions. However, when asked about complicated interventions, such as vasectomy and sclerotherapy of varicose veins, patients showed a clear preference for consultant care. The Ameland teleradiology study appears to be the first to use real patients and experiences; it is notable for highlighting that patients were extremely satisfied with the care substitution, showing trust in the abilities of primary care when supported by secondary care. Given the previous responses by patient groups, we expected patients to be reluctant and to prefer care by a radiologist and surgeon. When offered a more convenient diagnostic procedure on Ameland, patients showed trust in their GPs, although knowing that a hospital consultant was supervising the GP may have influenced this trust. For future projects introducing new technologies, it may be advisable to ensure greater patient involvement from the onset. After all, the success of novel care modalities is highly dependent on the faith that patients have in them, that is, unless insurance companies restrict the free choice of patients.

Finally, adequate funding is relevant. This thesis showed that the use of hospital facilities in general practice can lead to notable cost savings that are consistent with the government's austerity policy. Ultimately, the wide-scale introduction of diagnostic and treatment facilities in general practice should reduce the overall cost of care. However, success is conditional on there being clarity surrounding the funding of replacement, particularly where adjustment is needed to fit local needs. Lack of clarity or an ambiguous pay system could obstruct implementation, or even increase costs. It is also important to note that GPs funded the facilities in our project, adopting a fixed cost per treatment, in the spirit of entrepreneurship. Another feasible option would be for hospitals to provide financial support; however, the risk is that payment would be via the hospital DBC/DOT- system and would not reduce overall costs (see Box 1). Indeed, it may become more expensive.

Box 1

Since 2007, hospitals invoice their actions to insurance companies through the DBC- system (in English, Diagnosis Treatment Combination). These developments followed an agreement between hospitals, insurance companies, and the government in the Dutch system. This DBC-system is neither transparent nor controllable. The consequence was the development of the 'Project DOT' system (roughly translated as 'DBC's On Their Way to Transparency').

Similar issues would also apply for health insurers that wish to offer diagnostic and treatment services that fall between the needs of primary and secondary care in a separate centralized facility. Although this may be attractive, such an approach would increase the distance that many need to travel. It also remains uncertain if this would result in the desired cost savings, with the new structure requiring management, staff, and administration costs. It is essential to determine which option, a GP-led approach or a centralized facility, could provide the greatest benefit for the lowest cost before implementing it on a large scale. Given the scale of these costs, it is not only a social responsibility for GPs and consultants but it is also relevant for health insurers and politicians. GPs are uniquely placed to offer sensible, economical solutions to health care problems.

Strengths and limitations of the teleradiology study

Our teleradiology study is the first to assess unnecessary hospital trips, treatment, the accuracy of fracture diagnosis, and number of x-rays before and after the introduction of teleradiology in a general practice. Information was obtained on initial and final diagnosis, subsequent treatment, and number of x-rays made. The detailed description of the clinical signs and outcomes for trauma patients consulting a general practice before and after the introduction of teleradiology is consequently a major strength of this study. An additional strength is that the observed changes were not caused by differences in the x-ray examination procedures because all x-rays were interpreted by trained radiologists.

A limitation is that we did not carry out a randomized controlled experiment, for obvious ethical reasons. It is therefore possible that the difference in outcomes could be due to some factor other than the introduction of teleradiology. However, since the GPs, radiologists, surgeons, physical assistants, and procedures remained the same in 2006 and 2009, we think that the documented changes in outcomes were due to the

introduction of teleradiology. Indeed, because of changes in staff at the general practice and hospital radiology department in January 2010, we only compared two periods. Another limitation is that the cohorts in 2006 and 2009 were from different populations. Given that we could not contact all of the patients for follow-up, there may have been more missed fractures than were reported.

In the cost–benefit study, we consciously chose a theoretical control group (patients who would have had to go to the hospital without teleradiology) instead of comparing patients before and after the introduction of teleradiology. This was because we expected, as shown, that teleradiology would significantly affect decisions. The research also relied on one general practice setting with specific characteristics (located on a Dutch *Wadden*-island with a large tourist population).

The patient satisfaction study relied on a cross-sectional design, being conducted at a specific point in time, so we do not know the level of patient satisfaction before introducing the teleradiology service. Satisfaction with referral to the mainland hospital for an x-ray is also unknown. These facts preclude meaningful comparison and prevent us concluding whether patient satisfaction improved after the introduction of the teleradiology service, or whether there was truly greater satisfaction than with the usual hospital service. Nevertheless, the critical benefit of the teleradiology service was that it allowed patients to remain on the island and this study added to existing literature, by demonstrating that patients could accept GP-based services in the context of specialist support.

Another limitation was that questionnaire responses were only sought a short period after the x-ray was taken, which could have introduced bias. The adaptation of the original patient satisfaction questionnaire and the relatively high percentages of patients not answering certain items should also be considered limitations.

Future research, teleradiology, and care innovations

The research into care innovations in primary care and the replacement of care from hospitals to general practice is in its infancy in the Netherlands. The underlying research into teleradiology is limited to one GP practice that is at a distance from hospitals. Within this, the medical quality standards, cost benefits, and patient satisfaction have been the subject of study.

Medical quality

Medical quality can be assessed by missed diagnoses. One of the conditions required for hospital radiology services to be provided by GPs is that GPs provide equivalent quality to radiologists. All images in this study were assessed by radiologists and surgeons remotely, but it would be interesting to determine if GPs could match the

quality of assessment provided by specialists. This may require further academic training, and would be particularly important in settings where GPs are required to make a diagnosis unaided or when the Internet is not available. Indeed, some rural areas in Canada and Norway rely on GPs taking and assessing x-rays without supervision, and only sending images to a radiologist or referring the patient for further assessment in cases of doubt.

Research has highlighted a difference in assessment and evaluation by radiologists and non-radiologists, with current practice strongly in favor of all x-rays being assessed by radiologists [10]. While we endorse this principle, there are scenarios when a radiologist might not be readily available (for example at night) or when the continuity of hospital care cannot be guaranteed. Thus, we must know whether it is reasonable and safe for GPs to assess the x-ray images without the support of a radiologist. Indeed, this begs the question: is a digital link and radiology assessment a prerequisite for delivering the same standards of care as in hospital? We have already begun this research by presenting the same x-rays to a panel of radiologists and a panel of GPs, comparing the assessments, and checking the results with the known diagnosis. Teleradiology offers the opportunity for patients who are normally reliant on hospital care to be treated in general practice. Indeed, important diagnostic information can be obtained remotely and the data communicated digitally across the Internet; instead of patients needing to travel on real highways, key data can instead be transmitted via the electronic highway. It would be very interesting to investigate the potential of this electronic highway further, particularly in rural areas in the field of emergency care. We can consider here the introduction of computed tomography scans in general practice. Analogous to the treatment of fractures in domestic situations due to the introduction of teleradiology, thrombolysis for stroke patients could also be an option with the assistance of CT-scans. May be a little further is the introduction of the remote-controlled robot in general practice. However, first we must conduct further scientific research (quality standards, patient satisfaction, and cost benefits) before implementing any changes on a wider scale.

Costs and organization

It would be interesting to test our teleradiology results and findings on a much larger scale, and specifically in terms of comparing different organizational structures and researching the financial consequences. The implementation of hospital facilities in the general practice can be organized from the hospital or from the general practice. We have achieved this using an idealistic approach within general practice, resulting in fewer unnecessary hospital referrals, fewer missed diagnoses, considerable cost savings, and a greater number of satisfied patients. Following our initiative, hospitals

have reacted by using teleradiology in similar situations (e.g., Terschelling, Vlieland, and Lemmer). In these situations, the hospital is responsible not only for the facility but also for its management. Unlike on Ameland, where a medical fee can be charged, GPs on these other islands receive a surcharge on the registration fee. It would be interesting to do cost–benefit analysis comparing the two options, and specifically, whether the method of financing and management (i.e., hospital- or GP-led services) influences the cost. Several questions can then be raised: Would the increased medical fees lead to a greater number of investigations? Would hospital management lead to more referrals to the hospital and consequently more DBCs being opened? Would upcoding [11] be an issue (more expensive DBCs/DOTs being opened)? At the time of our study, health insurers did not have sufficient insight into the DBCs/DOTs charged by the hospital. Now that there is a desire to transfer hospital care facilities to primary care, they are actively trying to get this clarified. The latter is obviously conditional on doing a comparative study.

Patient satisfaction / patient experience

A great deal of research is required in the area of patient experience and satisfaction with care innovation and replacement. In relation to teleradiology, existing research has made no use of the consumer quality index (CQ-index), not least because it has only just been developed. In 2011, after five years' experience with this instrument, NIVEL stated that there were questions over its discriminatory power between institutions [12], and the debate around the standards against which the CQ-index results should be compared are ongoing. Although it is a good indicator of the standard of care experienced by patients, the validity of the CQ-index is still inadequately founded. Therefore, NIVEL concluded that a number of methodological questions require further attention.

It might still be too early to do further research because of the current doubts over the CQ-index. We therefore recommend that the evaluation of health care innovation and substitution be made on the basis of proven, well-validated patient satisfaction survey instruments. However, the CQ-index could be used as an instrument to check whether the standards of the GP practice itself are being met (in consultation with patients).

Guideline issues and research for general practice

In the above, we have summarized the results of the different aspects of this research and discussed the implications for care provision and future research. Next, we will consider the overarching themes of guideline revision and the implications for future

research from the perspective of an individual GP surgery.

Guideline implications

GPs working on islands are presented with problems that are not accounted for in the standard NHG guidelines. Despite the limitations of the existing guidelines, it has been demonstrated that each can be rectified with small adjustments. For example, we showed that change was needed to the basis of the guidelines for Lyme disease, that supplemental guidelines were necessary for Ameland disease in the management of gastroenteritis, and that additional services or provisions, such as teleradiology, could facilitate compliance with existing fracture management guidelines.

The Central Policy Organization (CBO, *Centraal Beleids Orgaan*) has used our research to support their guidelines. Supporting earlier research [13] that demonstrated Borrelia was not transmitted from a tick to an animal in the first 24 hours of a bite, we confirmed that this was also true in humans. In turn, this has led to the CBO advising against the administration of prophylactic antibiotics in their guidelines for the management of tick bites. Follow-up research has consistently shown that infection does not appear in the first 24 hours, with more than 24 hours' contact typically needed for infection [14]. There is an ongoing discussion between GPs, consultants, patient groups, and the CBO about whether or not prophylactic antibiotics should be prescribed if a tick is present on the skin for longer than 24 hours. Further research is advisable to develop meaningful guidelines.

As noted, there are important omissions from the guidelines for Lyme disease, gastroenteritis, and fracture management. While the NHG are yet to publish guidelines for the management of Lyme disease, the increased involvement of GPs mean that they are urgently needed. In addition, the discovery that raw milk is causative in Ameland disease requires the inclusion of this information in current NHG guidelines on the management of gastroenteritis; although attention is drawn to food in general as a cause of diarrhea, raw milk is not explicitly mentioned. Finally, distance to hospital is an important limiting factor when following the trauma guidelines for fracture management. Not only can the existing guidelines be met through teleradiology but we can also reduce the number of missed diagnosis and improve the overall quality of patient care. Although the existing guidelines have clear limitations, research such as ours should be used to remedy issues when noted. Indeed, an aim of the NHG is to ensure that guidelines remain up to date, with the association recently detecting 178 knowledge gaps in the 100 current NHG standards [15]. Although guidelines are based on scientific research where possible, the NHG increasingly recognizes that this is occasionally inadequate or even lacking.

The NHG, together with university general practice departments and NIVEL have

established an overview of all research concerning primary care in the Netherlands. In total, 187 surveys are being conducted to assess what research can be used to provide a solution for the existing knowledge gaps and to identify areas in which research is lacking. While the NHG focuses on institutional, large-scale research, this thesis has shown that small-scale research from single general practice surgeries can make important contributions to guidelines.

Implications for research

In the preceding section we highlighted that problems GPs are confronted with can be resolved through research. In this thesis, we have shown that not only were solutions found but also that the results extended beyond individual practice. Research from an individual GP surgery can contribute to changes in medical practice, improve our understanding of illnesses, and help develop cost-effective care through innovation; in short, it can help to develop the medical profession. This affirms the claim of MacKenzie (1908) who saw an important role for research by GPs in their own practices [16]. Similarly, in 2006, Green and Hickner indicated that such small-scale research could form the basis for larger studies in academic networks [17]. The research into ticks has proven to be a good example. After the results were published, RIVM adopted our model in 2008 and a nationwide follow-up study was initiated that included all Dutch general practice surgeries. The tick radar system was developed in such a way that allowed patients to send ticks directly to the RIVM without the need for GP intervention.

The teleradiology project is a good example of the evaluation of a healthcare innovation being implemented by GPs. In their "Future Vision 2022," both the NHG and the national general practitioners' association (LHV, *Landelijke Huisartsen vereniging*) showed that they are genuine supporters of research into innovations [18]. However, they are both of the opinion that the development and evaluation of pilot care innovations must first take place within academic networks, and only then be implemented and evaluated in daily practice. The question is whether it is appropriate to limit initiatives that start with GPs themselves; indeed, we suggest that by only allowing innovation and research to develop centrally, we may continue to generate guidelines with gaps for specific populations. Mainstream initiatives from primary care are therefore relevant and we should not rely solely on centrally developed plans for innovation. This is analogous to hospital medicine where individual teams make observations and perform limited research that helps direct larger studies. Waiting for a central agenda can delay progress and stifle innovation in primary care.

References

1. Rijpkema S, Nieuwenhuijs J, Franssen FF, Jongejan F**. Infection rates of *Borrelia burgdorferi* in different instars of *Ixodes ricinus* ticks from the Dutch North Sea Island of Ameland**. *Exp Appl Acarol* 1994;**18**:531-542.
2. Piesman J, Mather TN, Sinsky RJ, Spielman A. **Duration of Tick Attachment and *Borrelia burgdorferi* Transmission.** *J Clin Microbiol* 1987;**25**:557-558.
3. LCI. **Huisartsenkaart Lyme-borreliose.** Landelijke Coördinatiestructuur Infectiebestrijding. 1998. {Dutch)
4. Tweede Kamerbrief. **Reactie op advies 'Lyme onder de loep' van de Gezondheidsraad.** 29 augustus 2013, kenmerk 133987-107250-PG. (Dutch)
5. Mills JN, Gage KL, Khan AS, **Potential influence of climate change on vector –borne and zoonotic diseases: A review and proposed research plan**. *Environ Health Perspect* 2010;**118**(11): 1507-1514.
6. Nadelman RB, Nowakowski J, Fish D, Falco RC, Freeman K, McKenna D, et al. **Prophylaxis with single-dose doxycycline for the prevention of Lyme disease after an Ixodes scapularis tick bite.** *N Engl J Med* 2001;345:79-84.
7. www.zonmw.nl/nl/projecten/project-detail/tick-test-prophylaxis-proof/samenvatting.(Dutch)
8. Hubálek, Z., Halouzka, J., Juricová, Z. **Host-seeking activity of ixodid ticks in relation to weather variables.** *J. Vector Ecol* 2003; **28**(2): 159-165.
9. Van Dijk CE, Korevaar JC, de Jong JD, Koopmans B, van Dijk M, de Bakker DH. **Ruimte voor substitutie? Verschuivingen van tweedelijns naar eerstelijnszorg.** *NIVEL* 2013, ISBN 9789461222176. (Dutch)
10. Levin DC, Rao VM. Turf Wars in Radiology: **The Quality of Interpretations of Imagins Studies by Nonradiologist Physicians, A Patient Safety Issue?** *J Am Coll Radiol* 2004; **1**: 506-509.
11. Hasaart F. **Incentives in the Diagnosis Treatment Combination payment system for specialist medical care. A study about behavioral responses of medical specialists and hospitals in the Netherlands.** PhD thesis, University Maastricht 2011.

12. Hopman P, de Boer R, Rademakers J. **Kennisvraag: Wat heeft vijf jaar CQ-index opgeleverd?** NIVEL 2011. (Dutch)

13. Crippa M, Rais O, Gern L. **Investigations on the mode and dynamics of transmission and infectivity of *Borrelia burgdorferi sensu stricti* and *Borrelia afzezii* in *Ixodes ricinus* ticks.** *Vector Borne Zoonotic Dis* 2002;**183**:773-778.

14. Wilhelmson P, Lindblom P, Fryland L, Nyman D, Jaenson TGT, Forsberg P, Lindgren PE. **Ixodes ricinus ticks removed from humans in Northern Europe: seasonal pattern of infestation, attachment sites and duration of feeding.** *Paras Vectors* 2013;**6**:362.

15. Maassen H. **Kennislacunes huisartsgeneeskunde geïnventariseerd.** *Med Cont* 2014; **41**: 7 oktober 2014. (Dutch)

16. Moorhead R. **Sir James Mackenzie (1853-1952): views on general practice education and research.** *J R Soc Med* 1999; **92**: 38-43.

17. Green LA, Hickner J. **A Short History of Primary Care Practice-based Research Networks: From Concept to Essential Research Laboratories.** *JABFM* January-February 2006; **19**: 1.

18. NHG, LHV. **Toekomstvisie huisartsenzorg; modernisering naar menselijke maat. Huisartsenzorg in 2022.** Utrecht 2012.(Dutch).

Chapter 9

Summary

Summary

With the conduct of practice-based research, GPs can contribute to primary medical care practice, the development of the profession and our knowledge of disease processes. Such research need not be limited to clinical problems. GPs can play an important role in public health developments but also have the social responsibility to implement those developments which have been shown to be both medically successful and cost effective. This requires the use of both epidemiological and cost-benefit analyses.

This thesis describes three medical problems with which I was confronted as a GP on the island of Ameland (one of the Wadden islands north of the Netherlands). In the General Introduction (**Chapter 1**), I briefly outline the healthcare system in the Netherlands and the healthcare situation specific to the island of Ameland. In Part 1 or the epidemiological part of the thesis, I describe my research on the *Amelander Krankheit* and ticks. In part 2 or the innovative technology part, I present my research on the use and effectiveness of teleradiology.

Part I – Epidemiology*: 'Amelander krankheit'* and tick bites

Amelander krankheit

In a large area of Germany, children once suffered annually from the contagion *Campylobacter Jejuni*. The symptoms always arose after a stay on Ameland and the disease was therefore referred to as the *Amelander Krankheit* (Ameland disease). The NHG guideline for gastro-enteritis primarily focused on the diagnosis and treatment of this condition at the time and less on prevention. In other words, the preventive measures recommended by the guideline were not sufficient for the situation. All possible sources of bacteria were determined and excluded, but the ultimate source of the *C. jejuni* remained unknown. In **Chapter 2**, I describe the search for the source of *C. jejuni*, the discovery that the drinking of raw milk was the culprit and the conclusion that the slogan 'drinking milk (is good for you)' does not always hold.

Ticks

After the discovery of the mysterious Lyme disease in the early 1990s, the opinion was that the risk of acquiring this disease following a tick bite was very high. Especially those ticks living in the dunes were considered very dangerous. This belief spread even further via the media, which led us to investigate the actual transmission

of *Borellia Burgdorferi* (the bacterium which causes Lyme disease) by ticks to humans following a tick bite. In a prospective, observational study, we counted the number of infected ticks and, on the basis of this information, we calculated the probability of developing Lyme disease following a tick bite on Ameland. In retrospect, our study was the first in the Netherlands to link patients and ticks. In **Chapter 3**, I summarize the results of this research, which show that the chances of contracting Lyme disease following a tick bite are small if the tick is removed in time (approximately 1 in a 100); this is despite one-fifth of the ticks on Ameland being contaminated with *B. burgdorferi*. Indeed, the only infected patient in our research, during the research period of three years had a tick attached to the skin for more than 48 hours. The conclusions of this research support the existing treatment guidelines which recommend that antibiotics only be prescribed when clinical symptoms of Lyme borreliosis manifest themselves and not following every consult for a tick bite.

In **Chapter 4**, I further show in the same study with different analyses that the overall risk of developing clinical symptoms following a tick bite is just over 11% and that most of these symptoms are confined to local reactions. None of the participants in the study we conducted developed symptomatic Rickettsiosis, Babesiosis or Ehrlichiosis. The risk of overt symptomatic disease after a tick bite was lower than 0.5% in the study population. Although prompt removal of ticks reduces the risk of developing symptoms, the most powerful measure to avoid tick-borne diseases are preventive measures which include thorough checking for ticks, appropriate clothing, tick-avoidance behaviour and use of insect repellents.

Part II – Innovation: Teleradiology

Teleradiology

Distance to hospital can clearly be a barrier to the following of NHG guidelines. In situations where time is critical, GPs must obviously act quickly but specific knowledge and skills in addition to special diagnostic facilities may also be called for at times. To minimize treatment delays and avoid unnecessary trips to the a far-removed hospital , GPs often start treatment as soon as possible. Also in less acute situations involving — for example — fractures, a restrained referral policy is often adopted, which is counter to the existing NHG guidelines. This is done to prevent patients from having to make what often proves to be an unnecessary trip to the mainland hospital (i.e. return from the hospital with a diagnosis of `no fracture').

To reduce the risk of a missed positive diagnosis, our general practice purchased its own x-ray machine in 2007. All x-rays were then taken by a trained radiographer

employed by the general practice and digitally transmitted (teleradiology) to the closest hospital on the mainland (in Dokkum) for evaluation and interpretation by a radiologist. Several questions nevertheless arose with the adoption of this approach, including if the patients would accept and appreciate the local GP providing hospital services, if the same standard of care could be delivered as in the hospital and if the innovation would be cost effective for patients and society.

In **Chapter 5,** I describe the results of a retrospective, observational study showing that the use of teleradiology was clearly beneficial in terms of both reducing the number of missed fractures and increasing the potential for local treatment in the general practice rather than remote treatment in hospital . Fewer patients also had to make an unnecessary five-hour trip to the mainland hospital (i.e. travel only to hear 'no fracture'). The use of teleradiology thus had important consequences for both general practice diagnoses and treatment. Given that a greater number of patients could be treated locally, treatment delays were reduced. And although the number of x-rays increased, teleradiology made it easier for the GPs practicing far from a hospital to nevertheless comply with the relevant Dutch guidelines. This held particularly for patients with unclear clinical signs of fracture. In these cases, there were clearly less missed fractures, which showed the use of teleradiology to lead to a better quality of care.

In **Chapter 6**, I summarize the results of a cost-benefit analysis conducted for the year 2009 (i.e. the year in which the use of teleradiology in our local practice became fully operational). The economic investment and cost for the general practice, saved travel cost for the patients and teleradiology costs for health insurance organizations are compared to the costs which would have been incurred without teleradiology. The introduction of teleradiology produced a considerable cost reduction for both patients (€111,000 per year) and health insurance organizations (minimum of €89,000 per year) and small profit for the investor (in this case, the general practice).

In **Chapter 7**, I present the results of a cross-sectional study of the degree of satisfaction with the use of teleradiology among the vast majority of patients (including tourists) receiving an x-ray in the local general practice. Both the technical knowledge of the GPs with regard to the use of the teleradiology facility and the interpersonal communication between the doctors and radiographers with the patients) were rated high. Island residents were more satisfied than non-residents with the technical and interpersonal aspects of the care provided. Older patients and those with a non-trauma indication were also more satisfied than younger patients and those with a trauma indication. Although the above findings held for both the medical technical and interpersonal satisfaction subscales, the effects of age and

indication were most pronounced for the interpersonal scale. Sex, health status, level of education, past in-hospital experience with x-ray, and practice-based GP treatment versus hospital-based specialist treatment did not significantly influence the medical technical and interpersonal patient satisfaction. Not having to make the five-hour trip to the hospital was put forward as the most important argument in favour of teleradiology, with two-thirds of the respondents (66%) considering the time saving which this entails highly relevant (i.e. reduced travel time, faster diagnosis, faster treatment). Three-quarters of the respondents (75%) agreed that x-ray diagnosis need not always be conducted in the hospital.

In sum, the introduction of a teleradiology service into a general practice on the island of Amerland located north of the Netherlands reduced the number of missed fractures, reduced the number of unnecessary hospital referrals (i.e. trips to a distant facility) and increased local and thereby timely treatment of fractures. In addition, the introduction of teleradiology was positively valued by patients and produced a considerable savings for both health insurance companies and patients. Teleradiology is thus a good example of the cost-effective transfer of health care from hospital to primary healthcare centre.

General conclusion and recommendations

Finally, in **Chapter 8**, I summarize the insights provided by my research and offer some recommendations for future research and further practice. The strengths and limitations on the research reported here are summarized. The implications for care are spelled out. Possibilities for future research are suggested. And I conclude with some exploratory thoughts on the implications of our findings for the NHG guidelines but also the value of small-scale, general-practice research.

With regard to follow-up research on the spread of Lyme disease by ticks, I recommend the adoption of a multidisciplinary approach, more detailed evaluation of current prophylactic practices and investigation of where ticks flourish. '*Ameland Krankheit'* calls for research on other possible means of distribution (e.g. via drinking water or migratory birds). Our successful and cost-effective use of teleradiology should certainly be evaluated more widely, on a larger scale and in different organizational forms. In addition, the quality of the x-ray assessment done in the local general practice by GPs with that of the radiologists. Finally, I mention the need for further research on the possibilities of using the electronic highway in primary care (e.g. trombolysis or, in other words, clot busting for stroke patients, treatment via a remote-controlled robot by a specialist at a far removed hospitals, in addition to

research on other care innovations and the substitution of care. with the experiences and satisfaction of patients not forgotten when doing this.

In this thesis, small-scale research was shown to provide answers and solutions to local problems which can be characterized as bearing little or no association with larger research trends; the elusive cause of *Amelander Krankheit*, the transfer of *B. burgdorferi* and other tick-related diseases to humans and not being able to properly diagnose trauma patients. In a similar vein, back in 2006, Green and Hickner indicated that small-scale research can form the basis for larger-scale studies. The research on ticks reported on here is a good example of this. After the results were published, the National Institute for Public Health and the Environment in the Netherlands (*RIVM*) adopted our model, which subsequently led to the development of the tick radar system. As already mentioned, small-scale research such as that described in this thesis can also provide answers to larger, more general problems. Our research on the introduction of teleradiology, for example, is a good illustration of how healthcare can be transferred from hospitals to primary healthcare centres. Distance to the hospital was the local reason for the acquisition of an X-ray device by a primary healthcare centre. This option can be adopted by additional general practices as the group of remote practices grows as the outcome of the increased concentration of specialist care in a limited number of hospitals and thus creation of an increasing number of healthcare situation similar to that on the island of Amerland. Finally and also as mentioned, small-scale research can help use supplement and update the national healthcare guidelines in general (e.g. refine the guidelines with regard to milk consumption with gastroenteritis and cases of gastroenteritis; adjust policy on how to deal with tick bites).

In sum, the present research shows that some of the local problems GPs confront can be resolved with the conduct of a little research. The present research further shows that the results and solutions can often be extended beyond the individual practice then. Research from an individual healthcare centre can thus contribute to changes in medical practice, improve our understanding of illnesses and help develop cost-effective care via innovation. In short, small-scale research can help develop the medical profession. This confirms an important role for research in the work of GPs and gives us a good example of the evaluation of the healthcare innovations being implemented by GPs. In their Future Vision 2022, both the NHG (the Dutch College of General Practitioners; NHG, *Nederlands Huisartsen Genootschap*) and the LHV (the National GP association; LHV, *Landelijke Huisartsen vereniging*) have indicated that they are genuine supporters of research into healthcare innovation. However, they are both of the opinion that the development and evaluation of pilot

innovations should first take place in academic networks and only later be implemented and evaluated in daily healthcare practice. The question, of course, is whether initiatives starting with the GPs should be limited in such a manner or not. Shouldn't we welcome and recognize initiatives stemming from the field instead? Waiting for a central agenda may delay progress, stifle innovation and even miss crucial

Chapter 10

Nederlandse samenvatting

Nederlandse samenvatting

Door middel van onderzoek kunnen huisartsen zelf een bijdrage leveren aan de onderbouwing van het medisch handelen in de eerste lijn, aan het ontwikkelen van het vak en de kennis over ziektes. Daarbij moeten zij zich niet beperken tot hun klinisch georiënteerde taak. Huisartsen hebben ook een belangrijke rol in de volksgezondheid evenals een maatschappelijke verantwoordelijkheid om nieuwe ontwikkelingen in de zorg adequaat en kosteneffectief te implementeren. De eerste vergt een meer epidemiologische benadering, de tweede een innovatieve waarbij de kosten en baten ook van belang zijn om mee te wegen.

Dit proefschrift beschrijft drie specifieke medische problemen waarmee ik geconfronteerd werd in mijn huisartsenpraktijk op Ameland (een van de Waddeneilanden). In het inleidende **hoofdstuk 1** presenteer ik kort het Nederlandse gezondheidszorgsysteem en de specifieke zorgsituatie op het eiland. Daarnaast introduceer ik de drie onderzoeksgebieden ('Amelander Krankheit', teken en teleradiologie) en de onderzoeksvragen. Deel 1 van dit proefschrift beschrijft de onderzoeken over de 'Amelander Krankheit' en de teken (het epidemiologisch deel) en deel 2 de onderzoeken over teleradiologie; het deel waarin een innovatie wordt onderzocht) waarbij gekeken is naar zowel medische-, economische- als sociale aspecten.

Deel 1 – 'Amelander Krankheit' en Tekenbeten

'Amelander Krankheit'

In een groot gebied rond Keulen in Duitsland kwam jaarlijks een gastro-enteritis epidemie voor bij kinderen als gevolg van een besmetting met de C*ampylobacter jejuni*. De ziekteverschijnselen ontstonden altijd na een verblijf van de kinderen op Ameland en werd daarom in de Duitse volksmond de "Amelander Krankheit" genoemd. Alle mogelijke genoemde bacteriebronnen werden achterhaald en uitgesloten, maar de uiteindelijke bron van de C. *jejuni* bleef onbekend. Achteraf bezien blijkt dat we ons teveel focusten op voor de hand liggende bronnen, zoals bijvoorbeeld te rauw kippenvlees bij barbecue. **Hoofdstuk 2** beschrijft de speurtocht naar de bron van C. *jejuni:* uiteindelijk bleek dit rauwe melk te zijn. Het devies dat het drinken van melk gezond is, klopt dus niet altijd. Het is van belang rauwe melk als mogelijk oorzaak in de anamnese meet te nemen.

Teken

In de negentiger jaren van de vorige eeuw was men, na de ontdekking van de mysterieuze ziekte van Lyme, ervan overtuigd dat er een erg hoog risico bestond op het krijgen van deze ziekte na een tekenbeet. Met name de teken in de duinen waren het meest risicovol. Deze overtuiging vormde zelfs een belangrijk item in de media. Voor ons was dit aanleiding om een onderzoek te starten naar de werkelijke overdracht van *Borellia Burgdorferi* (de bacterie die de ziekte van Lyme veroorzaakt) door de teek naar de mens na een tekenbeet. Het betrof een prospectief observationeel onderzoek met als doel het aantal geïnfecteerde teken en de kans op het ontstaan van de ziekte van Lyme na een tekenbeet op Ameland te achterhalen. Achteraf bezien blijkt dit het eerste onderzoek in Nederland te zijn waarin patiënten aan teken zijn gekoppeld.

Hoofdstuk 3 schetst dit onderzoek en laat zien dat de kans op het daadwerkelijk krijgen van de ziekte van Lyme na een tekenbeet op Ameland gering is (< 1%), ofschoon een relatief groot percentage van de teken geïnfecteerd is met *B.burgdorferi* (20,4%). Deze geringe overdracht hangt waarschijnlijk samen met het feit dat in de meeste gevallen de teek binnen 24 uur verwijderd is. Onze bevindingen ondersteunen de CBO-richtlijn om antibiotica alleen voor te schrijven bij klinische verschijnselen van Lyme borelliose, en niet na iedere tekenbeet.
Omdat enerzijds uit de enquête naar voren kwam dat veel patiënten met name huidklachten kregen na een tekenbeet en anderzijds het laboratorium liet zien dat de teken naast de *B. burdorferi* ook andere bacteriën *(o.a. Rickettsia, Babesia en Ehlicha)* bevatten hebben we het onderzoek herhaald met de vraag of de bovengenoemde klachten van de patiënten verklaard konden worden door besmetting met deze andere bacteriën.

Hoofdstuk 4 beschrijft het onderzoek waarbij gebruik gemaakt is van de gegevens van hoofdstuk 3 aangevuld met data uit een extra jaar onderzoek en laat zien dat de kans op het krijgen van symptomen na een tekenbeet 11.4% is. Dit zijn meestal huidreacties. Tevens laat het zien dat de kans op het krijgen van Lyme borreliosis, ricketsiosis, babesiosis of erhlichiosis na een tekenbeet kleiner dan 1 % is in deze studie populatie. Het zo snel mogelijk verwijderen van teken na een tekenbeet vermindert het risico op het krijgen van teek gerelateerde ziekten. Het goed controleren van het lichaam samen met het dragen van beschermende kleding, teek vermijdend gedrag en het gebruik van insecten werende middelen zijn de meest effectieve maatregelen om teken gerelateerde ziektes te voorkomen.

Deel 2 – Teleradiologie

De afstand tot het ziekenhuis vormt soms een barrière om de NHG-richtlijnen te kunnen volgen. Zeker in acute situaties waarin de factor tijd cruciaal is, is de huisarts op grote afstand van het ziekenhuis, zoals op een eiland, genoodzaakt tot direct handelen. Naast specifieke vaardigheden zijn vaak extra diagnostische voorzieningen vereist. Om vertraging van de behandeling te voorkomen en patiënten niet te belasten met een (achteraf gezien) onnodige reis naar het ziekenhuis, zal de huisarts waar mogelijk zelf de diagnostiek en behandeling ter hand nemen en in gang zetten.

Ook in minder acute situaties, zoals in het geval van fracturen, wordt in afwijking van de NHG richtlijnen een terughoudend verwijsbeleid gevoerd om te voorkomen dat patiënten onnodig belast worden met een trip naar het ziekenhuis om vervolgens onverrichter zake met de diagnose 'geen fractuur' terug te keren. Om het risico van gemiste diagnoses te vermijden is in 2007 door onze praktijk een röntgenapparaat aangeschaft. De röntgenfoto's worden gemaakt op het eiland in onze huisartsenpraktijk en digitaal verstuurd naar het ziekenhuis en beoordeeld door de radioloog. Vervolgens vindt communicatie plaats over diagnose en beleid met radiologen en/of chirurgen. De vraag is of patiënten een dergelijke ziekenhuisvoorziening in een huisartsenpraktijk waarderen en accepteren, of dezelfde medische kwaliteit als die van het ziekenhuis kan worden geleverd en of deze innovatie vanuit maatschappelijk perspectief gezien kosteneffectief is.

Hoofdstuk 5 beschrijft een retrospectieve, observationele studie waarbij alle trauma patiënten, die de huisartsenpraktijk bezochten in 2006, dus vóór de introductie van teleradiologie in de huisartsenpraktijk, vergeleken zijn met alle trauma patiënten in 2009, na de introductie van teleradiologie.

In 2006 en 2009 bezochten 312 respectievelijk 482 patiënten met een trauma de huisartsenpraktijk, waarvan 66 respectievelijk 116 patiënten met een fractuur en/of luxatie. In 2006 zijn 9 fracturen gemist, in 2009 zijn 2 fracturen gemist. In 2006 werden 15 patiënten met een fractuur of luxatie in de huisartsenpraktijk behandeld, in 2009 waren het er 77. In 2006 zijn er 41 patiënten onterecht naar het ziekenhuis verwezen tegen 2 in 2009. Deze studie laat zien dat na de introductie van de teleradiologie minder fracturen gemist worden, dat er minder patiënten onterecht verwezen worden naar het ziekenhuis en dat er patiënten in de huisartsenpraktijk behandeld zijn, die normaal in het ziekenhuis behandeld worden.

Hoofdstuk 6 laat een kosten-baten analyse zien van het jaar 2009 (teleradiologie volledig operationeel zonder kinderziekten) waarbij de bedrijfseconomische kosten, de bespaarde reiskosten en reistijd van de patiënt en de teleradiologiekosten van de ziektekostenverzekeraar vergeleken worden met de kosten die gemaakt zouden zijn zonder teleradiologie.

Er zijn in de huisartsenpraktijk 426 röntgenonderzoeken uitgevoerd, waarvan 241 voor trauma's en 185 voor andere klachten. Met een vergoeding van €100 per onderzoek tijdens kantooruren (€200 in de avond- en weekenddienst) bedroegen de baten voor de huisarts (financier van het röntgenapparaat) in 2009 bijna €980. De in het onderzoek betrokken patiënten (426) besparen in totaal omgerekend €111.068 aan reistijd en -kosten. En de in het onderzoek betrokken ziektekostenverzekeraars zijn minimaal €89.265 goedkoper uit voor diagnose en behandeling. Kortom, de introductie van teleradiologie in een huisartsenpraktijk op Ameland leidt tot aanzienlijke kostenbesparingen voor zowel patiënten als ziektekostenverzekeraars

Hoofdstuk 7 geeft een cross-sectioneel onderzoek weer, waarbij alle patiënten, die een röntgenfoto hebben laten maken in de huisartsenpraktijk tussen 1 juni 2007 en 1 juni 2009, een vragenlijst gebaseerd op de Nederlandse versie van de Patient Satisfaction Questionnaire III (PSQ.NL) kregen toegestuurd. Het respons percentage bedroeg 65%, wat hoog mag worden genoemd. De tevredenheid over de medisch technische kwaliteit van de professionals met teleradiologie in de huisartsenpraktijk was erg hoog, evenals de tevredenheid over de interpersoonlijke begeleiding van de patiënt. Uit de analyse blijkt dat eilandbewoners tevredener zijn met de medisch technische- en interpersoonlijke vaardigheden van de huisarts en/of radiologisch laborante dan niet-eilandbewoners. Dit geldt ook voor de ouderen en patiënten zonder trauma indicatie ten opzichte van de jongere patiënten en patiënten met een trauma indicatie.

Discussie en Conclusies

Tenslotte vat **hoofdstuk 8** de conclusies en aanbevelingen samen. Tevens schetsen we de beperkingen en sterke punten van de onderzoeken, beschrijven we de implicaties voor de zorg en de mogelijkheden van toekomstig onderzoek. We eindigen het hoofdstuk met wat verkennende gedachten over de eventuele impact van het onderzoek op de NHG-richtlijnen en over de waarde van het kleinschalige onderzoek vanuit de huisartsenpraktijk.

Wat het vervolgonderzoek rond teken en Lyme betreft zijn we voorstander voor een multidisciplinaire aanpak, een evaluatie van het huidige profylaxe beleid en te gaan onderzoeken waar teken het best gedijen. Voor de Amelander Krankheit zou nader onderzoek naar de wijze van verspreiding (via drinkwater of trekvogels) wenselijk zijn. In het deel waarin het toekomstig onderzoek rond teleradiologie is opgenomen, pleiten we er voor om onze bevindingen op grotere schaal te toetsen, waarbij verschillende organisatie -vormen worden vergeleken evenals hun financiële consequenties. Ook zou het aardig zijn de kwaliteit van het beoordelen van de foto's door de huisartsen te vergelijken met die van de radiologen. Als laatste noemen we onderzoek naar de verdere mogelijkheden van de elektronische snelweg in de huisartsenzorg (trombolyse van stroke-patienten, behandeling met remote-controlled robot) plus dat er nog veel onderzoek gewenst is naar zorginnovaties en substitutie, waarbij de patiëntenervaringen/satisfactie vooral niet mag worden vergeten.

Dit proefschrift laat zien dat wanneer geen aansluiting gevonden kan worden op lopend onderzoek, kleinschalig onderzoek, antwoorden en oplossingen biedt voor de lokale problemen de onvindbare oorzaak van 'Amelander Krankheit', de overdracht van *B. burgdorferi* en andere teek gerelateerde ziekten door teken naar de mens en het niet goed kunnen diagnosticeren van trauma patiënten. Daarnaast toont het aan dat het kleinschalige onderzoek een basis vormt, zoals Green en Hickner (2006) beschrijven, voor grootschalig onderzoek. Zo is het Amelandse tekenonderzoek overgenomen door het RIVM en op nationaal niveau uitgevoerd, wat uiteindelijk heeft geleid tot het landelijke tekenradar onderzoek. Ook kan het kleinschalig onderzoek zoals beschreven in dit proefschrift ook een antwoord geven op grotere niet-lokale issues. Zo leidt ons onderzoek naar de introductie van teleradiologie *(hoofdstuk 5-7)* tot de conclusie dat teleradiologie een goed voorbeeld is van substitutie van zorg van de tweede- naar de eerste lijn. Afstand tot het ziekenhuis vormde de lokale aanleiding om tot aanschaf van röntgenapparatuur over te gaan. Echter teleradiologie kan ook een goede optie zijn voor perifere huisartsenpraktijken en huisartsenposten die door de fusies van ziekenhuizen steeds verder van een ziekenhuis komen te liggen en in een situatie terechtkomen die dan te vergelijken is met de eiland situatie. Tenslotte kan kleinschalig onderzoek bijdragen aan de aanvulling en actualisering van de NHG-richtlijnen in algemene zin (bv. vragen naar drinken van rauwe melk bij gastro-enteritis en het beleid bij een tekenbeet).

Het voorgaande laat zien dat vragen en problemen waarmee een huisartsenpraktijk wordt geconfronteerd beantwoord en opgelost kunnen worden aan de hand van onderzoek. Dit proefschrift toont aan dat niet alleen oplossingen werden gevonden maar ook dat het resultaat verder reikte dan de eigen praktijk: het onderzoek vanuit

de eigen huisartsenpraktijk heeft bijgedragen aan de onderbouwing van het medisch handelen, de kennis over ziektes en de evaluatie van zorginnovaties/het adequaat kosteneffectief ontwikkelen van de zorg. Kortom aan de ontwikkeling van het vak. Dit bevestigt de stellingname, dat naast het grootschalige onderzoek een belangrijke rol is weggelegd voor onderzoek door huisartsen in hun eigen praktijken.

Het is een voorbeeld van een evaluatie van de implementatie van een zorginnovatie in de dagelijkse praktijk. In hun toekomstvisie 2022 tonen de NHG en de LHV zich grote voorstanders van onderzoek naar innovaties. Zij vinden echter dat de ontwikkeling en evaluatie van pilots van zorginnovaties eerst in de academische netwerken moeten plaatsvinden om vervolgens in de dagelijkse praktijk te worden geïmplementeerd en geëvalueerd. De vraag is echter of we daarmee de initiatieven in het veld niet teloor laten gaan. De vraag is dan ook of we in Nederland initiatieven in het veld, vanuit de eerste lijn zelf, niet meer moeten koesteren en honoreren vooraleer over te gaan op het centraal vaststellen van een innovatie-agenda? Het wachten op een centrale agenda kan weleens vertragend werken en innovaties vanuit de eerste lijn in de weg staan.

Dankwoord

Dankwoord

Een proefschrift schrijven naast patiëntenzorg, opleiding en onderwijs, is geen sinecure. Zonder de bijdragen en steun van velen was dit boekwerk niet tot stand gekomen. Wat eigenlijk begon met een radiobericht, waarin een microbioloog beweerde dat het voor toeristen erg gevaarlijk was om op de Waddeneilanden te verblijven vanwege de grote kans op de ziekte van Lyme , en een artikel in het blad de Entrepreneur, waarin beweerd werd dat de huisartsen in het noorden niet innovatief en ondernemend zijn en een oude melkbuis, waar later een glasvezelkabel doorgetrokken is, is langs een weg van onderzoek geëindigd in dit proefschrift.

Allereerst wil ik de patiënten (Amelanders en passanten) bedanken die het vertrouwen in ons stelden en wilden meewerken aan het onderzoek en de innovatie. Ik ben mijn begeleiders erg dankbaar voor het vertrouwen dat ik van hen heb gekregen.
Prof. dr. R. Sanderman, als eerste promotor. Beste Robbert, het wekelijks overleg heb ik als zeer prettig en leerzaam ervaren. Jouw snelle denken, geduld en geloof in het project vind ik nog steeds bewonderenswaardig. Evenals jouw lef om van het gebaande pad af te wijken en je te begeven op een ander vakgebied. En het allerbelangrijkste is misschien wel dat je er stond op het moment dat we een kleine tegenslag hadden. Ik heb dat als een enorme stimulans en steun ervaren.
Prof. dr. T. van der Molen, als tweede promotor. Beste Thys, je bent later in het project gestapt. Ook bij jou kon ik zo binnenvallen. Je gaf me zelfs het gevoel dat je jouw 'vrije' vrijdag speciaal voor mij vrijmaakte. Bij jou vond ik gehoor en een gedeelde 'rurale' belangstelling. Het was prettig dat je jouw kennis van het huisartsenvak, in de breedste zin van het woord, met me wilde delen. Dat heb ik als een enorme steun ervaren.

Dr. J.P.A.M. Jacobs. Beste Jan, jij bent degene die me heeft ingewijd in de geheimen van de wetenschap. Door mij op een subtiele en bijna onuitputtelijk wijze aan te sporen, hield je het tempo erin. Ik bedank je voor jouw belangrijke inhoudelijke bijdrage, de structuur, het spiegelen en de continue druk op de ketel. Gelukkig zorgde je ook voor de broodnodige ontspanning. De opmerking: "Het is hier al 17.00 uur" (voor ons het tijdstip om een Leffe Dubbel te drinken) heb ik toch vele malen al om 16.00 uur gehoord.

Special thanks to the members of the reading committee prof. dr. C (Christos) Lionis, prof. dr. J.C. (James) Coyne and prof. dr. N.H. (Niels) Chavannes. Thank you so much for reading and approving the manuscript.

Collega Monique, alle medewerkers (Cilia, Jetske, Pieternel, Britta, Mariska, Anneke, Karen, Jellie, Jaap en Trudie) en ex-medewerkers (Cyrilla, Greetje, Joke, Anne en Marian). Jullie hebben me de ruimte gegeven om het huisartsenvak in de volle breedte te kunnen uitoefenen, zodat ik naast patiëntenzorg en opleiding ook onderzoek kon doen. Daarnaast hadden jullie het geduld om de teken te versturen, traden jullie de teleradiologie met open vizier tegemoet en verstonden jullie de kunst om deze techniek snel eigen te maken. Hartstikke bedankt hiervoor. Ik ben trots op jullie.

Het proefschrift beschrijft drie onderzoeken, waaraan velen hebben meegewerkt. Hen wil ik graag bedanken voor hun bijdrage.
Teken
Jon Brouwers, jij was huisarts-in-opleiding. Gezamenlijk hebben we het tekenonderzoek opgezet. Jammer dat je later niet meer de tijd had om van het vervolg te genieten. Jan Schuling, door jouw enthousiasme over de opzet wisten Jon en ik dat deze goed was.
Afke Brandenburg en Gerda Noordhoek (Izore, Leeuwarden): jullie, bedankt voor de goede samenwerking, het brainstormen en het promoten van ons onderzoek en de resultaten ervan op wetenschappelijke bijeenkomsten.
John Ekkelboom, jij voor de vertaalslag van de wetenschappelijke bevindingen naar het publiek, wat de nodige publiciteit heeft opgeleverd.
Teleradiologie
Jan Hamel, voormalig voorzitter van de Raad van Bestuur van het UMCG. Mijn dank omdat hij zonder het zelf te weten heeft gefungeerd als inspiratiebron. Ten eerste vanwege zijn visionaire blik op de toekomst van de zorg en het feit dat hij, ver voordat anderen erover gingen filosoferen, al samenwerking tussen de eerste en tweede lijn stimuleerde. Ten tweede omdat hij ten tijde van de marktwerking in de zorg Rianne naar Amerika liet gaan om de gezondheidszorg daar te bestuderen. Beide hebben als input voor mijn proefschrift gediend.

Francis Fullam (Rush Medical Centre, Chicago): thank you very much for the brainstorming about patient satisfaction and patient experience.
Marina Beckers, jij hebt je enorm ingezet voor de enquête onder de patiënten. Je nam niet alleen de administratieve uitvoering ter hand, maar je hebt ook de resultaten gebundeld en ervoor gezorgd dat de respons zo hoog was.

De Friesland Zorgverzekeraar: Jan van der Meulen, Irene van der Meer, Lianne van der Meer, Laurence Kea en de heer Feenstra die hun nek durfden uit te steken en het project met middelen van het Innovatiefonds mogelijk maakten. Rob Kooiker,

Inge Dijkstra en Ursula de Jonge Baars die het stokje overnamen en voortzetting mogelijk maakten.

Frits Pol, Adviesgroep Noord: zonder jouw tact en zakelijkheid tijdens de financiële onderhandelingen op de moments suprêmes was het project nooit gelukt. Bedankt voor jouw enorme inzet.
Jos Zegers: Tot tweemaal toe hebben we gebruik moeten en mogen maken van jouw netwerk. Bedankt voor jouw lobby waardoor de financiering van teleradiologie door de zorgverzekeraars behouden bleef.

De Sionsberg:
Jan Feddema, Peter Fahner, Floris van Moppes, Niels van Lindert, Maurice van Hillo, Sharon Muller en andere medewerkers van de afdeling Radiologie die, vele jaren voorafgaand aan de substitutieplannen in 2015, bereid waren om met ons samen te werken, en hun kennis met ons te delen. Heel erg bedankt en ik hoop dat we het project kunnen voortzetten na de tegenslagen die jullie ziekenhuis heeft gehad.

RUG/UMCG:
Frank Baarveld, in het begin hebben we intensief samengewerkt en gebrainstormd over de opzet en uitvoering van het onderzoek. Door omstandigheden konden we dit helaas niet samen afronden. Ik wil je ook bedanken voor de ondersteuning die jij als hoofd van de huisartsenopleiding mij hebt geboden met de inzet van Jannie Stellingwerff, Chantal Visser, Anita Verhoeven en Renze Hasper.
Truus van Ittersum, je bent een kei en niet te evenaren in het snel en effectief zoeken in allerlei literatuurprogramma's. Ik heb daar veel profijt van gehad. Als bijzonder eervol heb ik het ervaren dat jij jouw kamer voor mij wekelijks beschikbaar stelde. Bedankt hiervoor en ik hoop dat ik nog lang van jouw kwaliteiten en faciliteiten gebruik mag maken.
Eric van Sonderen, bedankt voor het onderwijs in de methodologie. Je hebt enorm veel geduld, bent ontzettend enthousiast, hebt een kritische blik en wat ik eveneens erg waardeer is dat je nooit vastgeroest zit aan kantoortijden. Zelfs buiten je werktijd om, vaak in een wat andere ambiance, heb ik veel kennis opgedaan over wetenschappelijk onderzoek.
Renate Kroese, bedankt voor jouw hulp bij mijn start op de afdeling. Jammer genoeg heb ik door je promotie naar de zesde verdieping slechts kort kunnen genieten van jouw steun.
Annemieke Brouwers en Carin Buijvoets, bedankt voor jullie ondersteuning. Het mooie was dat ik er zelden om hoefde te vragen.

Alle andere collega's van de vijfde verdieping wil ik bedanken voor de aangename sfeer en het welkome gevoel dat jullie mij hebben gegeven.

Naast de steun in de wetenschap heb ik ook op andere terreinen steun ervaren, waardoor mij tijd werd bespaard en ik ruimte kreeg om aan het onderzoek te kunnen werken.
Jan en Duan Jacobs: het was fijn om jullie elk jaar in november in Thailand te bezoeken. Het regelmatig golfen heeft niet zozeer tot het verbeteren van mijn handicap geleid, maar heeft wel een gunstige invloed gehad op mijn werkprestaties. Bedankt voor het sublieme werkadres en het overheerlijke voedsel.

Anton, mijn buurman, wil ik bedanken voor de opvang van mijn paarden. Elke donderdag en vrijdag, wanneer ik in het UMCG vertoefde, stond hij voor ze klaar: zij zijn niets tekortgekomen.

Durk en Benne, jullie voor het trouw klaarzetten van mijn vliegtuig, zodat ik vliegensvlug naar de wal kon gaan.

Gjok Oe (chirurg) en Jos Geling (gynaecoloog): van jullie heb ik de klinische vaardigheden geleerd, waardoor ik de grenzen van het huisartsenvak kon opzoeken. Ik vind het fijn dat jullie beiden nog op Ameland zijn geweest om het resultaat te beoordelen. Het is jammer dat jullie de promotie niet meer kunnen meemaken.

Mijn vader en moeder wil ik bedanken voor het doorzettingsvermogen dat ze aan mij hebben overgedragen. En mijn moeder, balancerend tussen de eerste- en tweede lijn, omdat je met jouw instructies aan zowel de cardioloog als de huisarts, tot het laatst er alles aan hebt gedaan om te overleven en dit historisch moment mee te kunnen maken.

Janny, bedankt dat Jan, naast het paardrijden, zoveel tijd kreeg om met mij van gedachten te wisselen over het onderzoek.

Mijn zus Ineke en Herman, het is fijn om jullie als paranimfen te hebben. Het is bewonderenswaardig hoe jullie beiden het paranimfschap wisten te combineren met jullie drukke banen. Ineke, in 2003/2004 heb je onze praktijk tijdens het hoogseizoen twee maanden lang enorm uit de brand geholpen en veel werk voor ons verzet. De manier waarop jij in stressvolle situaties het hoofd koel hield en de sfeer goed wist te houden, vond ik opvallend. Het voelt dan ook als zeer vertrouwd om jou weer aan mijn zijde te hebben. Herman, het is mooi dat we na 25 jaar, aanvankelijk tweewekelijks en later wekelijks brainstormend over ons vak in de Wolthoorn en bij

de Vietnamees, nu bij de verdediging samen mogen staan: nog steeds als de ‘jonge’ enthousiaste huisartsen.

Rianne, bedankt voor jouw geduld en steun, het blijven geloven in ons ideaal, jouw corrigerende opmerkingen met name als ik weer qua tekst ‘erg kort door de bocht ging’ en het inleveren van veel vakanties en vrije tijd. Ik hoop dat we nog heel lang van elkaar kunnen genieten en dat de eerstvolgende vakantie dit alles ruimschoots compenseert.

Curriculum Vitae

Op 1 juli 1991 heeft Jac. Jacobs zich gevestigd als huisarts in Ballum op Ameland. Als voorbereiding heeft hij de Huisartsopleiding in Nijmegen gedaan met de huisartsenpraktijk “de Vier Kwartieren” in Boxtel als opleidingspraktijk. Vooraf aan de huisartsopleiding heeft hij de tropenopleiding (KIT) doorlopen met als praktijklocaties St. Jozefziekenhuis te Kerkrade (afdeling chirurgie), RKZ te Groningen (afdeling gynaecologie). Gedurende de huisartsenopleiding heeft hij zijn chirurgische- en gynaecologische vaardigheden op niveau gehouden in het Lidwinaziekenhuis te Boxtel (afdeling chirurgie en afdeling gynaecologie).

Op Ameland biedt hij zorg aan de eilanders van ‘de wieg tot het graf’ ofwel richt hij zich op thuisbevallingen tot en met stervensbegeleiding. In verband met de lange afstand naar het ziekenhuis streeft hij ernaar de mensen zo lang mogelijk thuis te houden en in de eerste lijn te behandelen. Uiteraard blijven verwijzingen naar specialisten noodzakelijk.

Om de kwaliteit te waarborgen is hij in 1991 gestart met substitutie van het ziekenhuis naar de eerstelijn en innovaties (ECG- , echo- en later röntgenonderzoek) in nauwe samenwerking met specialisten. Een aantal specialisten (kinderarts, cardioloog, oogarts en specialist ouderen geneeskunde) komen zelfs naar het eiland toe voor consultatie en houden spreekuur in de huisartsenpraktijken. Verder is de praktijk verbonden aan de Huisartsopleiding van het UMCG (Groningen) en de VU (Amsterdam). Samen met het UMCG verricht Jacobs wetenschappelijk onderzoek.

Regelmatig wordt hij gevraagd om voor collega’s (huisartsen en specialisten) op te treden. Tot slot mag vermeld worden dat hij en zijn associé samen met de Huisartsopleiding van het VUMC een speciaal curriculum hebben ontwikkeld voor de opleiding tot eilanddokter.

List of SHARE previous presentations

Research Institute SHARE

This thesis is published within the **Research Institute SHARE** (Science in Healthy Ageing and healthcaRE) of the University Medical Center Groningen / University of Groningen.
Further information regarding the institute and its research can be obtained from our internetsite: http://www.share.umcg.nl/

More recent theses can be found in the list below.
((co-) supervisors are between brackets)

2016

Otter TA
Monitoring endurance athletes; a multidisciplinary approach
(prof KAPM Lemmink, prof RL Diercks, dr MS Brink)

Bielderman JH
Active ageing and quality of life; community-dwelling older adults in deprived neighbourhoods
(prof CP van der Schans, dr MHG de Greef, dr GH Schout)

Bijlsma MJ
Age-period-cohort methodology; confounding by birth in cardiovascular pharmacoepidemiology
(prof E Hak, prof S Vansteelandt, dr F Janssen)

Dingemans EAA
Working after retirement; determinants and conzequences of bridge employment
(prof CJIM Henkens, dr ir H van Solinge)

Jonge L de
Data quality and methodology in studies on maternal medication use in relation to congenital anomalies
(prof IM van Langen, prof LTW de Jong-van den Berg, dr MK Bakker)

Vries FM de
Statin treatment in type 2 diabetes patients
(prof E Hak, prof P Denig, prof MJ Postma)

Jager M
Unraveling the role of client-professional communcation in adolescent psychosocial care
(prof SA Reijneveld, prof EJ Knorth, dr AF de Winter, dr J Metselaar)

Mulder B
Medication use during pregnancy and atopic diseases in childhood
(prof E Hak, prof SS Jick, dr CCM Schuling-Veninga, dr TW de Vries)

Romkema S
Intermanual transfer in prosthetic training
(prof CK van der Sluis, dr RM Bongers)

Diest M van
Developing an exergame for unsupervised home-based balance training in older adults
(prof GJ Verkerke, prof K Postema, dr CJC Lamoth, dr J Stegenga)

Waterschoot FPC
Nice to have or need to have? Unraveling dosage of pain rehabilitation
(prof MF Reneman, prof JHB Geertzen, prof PU Dijkstra)

Zijlema WL
(Un)healthy in the city; adverse health effects of traffic-related noise and air pollution
(Prof JGM Rosmalen, prof RP Stolk)

Zetstra-van der Woude AP
Data collection on risk factors in pregnancy
(prof LTW de Jong-van den Berg, dr H Wang)

Mohammadi S
The intersecting system of patients with chronic pain and their family caregivers; cognitions, behaviors, and well-being
(prof M Hagedoorn, prof R Sanderman, dr M Deghani)

Verbeek T
Pregnancy and psychopathology
(prof MY Berger, prof CLH Bockting, dr H Burger, dr MG van Pampus)

2015

Broekhuijsen K
Timing of delivery for women with non-severe hypertensive disorders of pregnancy
(prof PP van den Berg, prof BWJ Mol, dr MTM Faassen, dr H Groen)

Tuuk K van der
Who's at risk? Prediction in term pregnancies complicated by hypertensive disorders
(prof PP van den Berg, prof BWJ Mol, dr MG van Pampus, dr H Groen))

Vitkova M
Poor sleep quality and other symptoms affecting quality of life in patients with multiple sclerosis
(prof SA Reijneveld, prof Z Gdovinova, dr JP van Dijk, dr J Rosenberger)

Sudzinova A
Roma ethnicity and outcomes of coronary artery disease
(prof SA Reijneveld, dr JP van Dijk, dr J Rosenberger)

For more 2015 and earlier theses visit our website